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Publication date:
2013

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COLOFON

Sijtsma, A.
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Dissertation University of Groningen, with summary in Dutch

ISBN: 978-90-367-6256-4

Cover photo and design: Anna Sijtsma
Lay-out: Anna Sijtsma
Printed by: Ipskamp drukkers, Enschede

The Gecko Drenthe birth cohort study presented in this thesis was financially supported by Kruidvat (Hutchison Whampoa Ltd), University of Groningen, University Medical Center Groningen, Well Baby Clinic Foundation ICARE, Menzis, Noordlease and GGD Drenthe.

The printing of this thesis was financially supported by the Graduate School of Medical Sciences SHARE, University Medical Center Groningen, University of Groningen and the Netherlands Association for the Study of Obesity.

RIJKSUNIVERSITEIT GRONINGEN

Physical activity and overweight in young children

Proefschrift

ter verkrijging van het doctoraat in de
Medische Wetenschappen
aan de Rijksuniversiteit Groningen
op gezag van de
Rector Magnificus, dr. E. Sterken,
in het openbaar te verdedigen op
dinsdag 25 juni 2013
om 11.00 uur

door

Anna Sijtsma

geboren op 6 januari 1986
te Dokkum

Promotores:	Prof. dr. P.J.J. Sauer Prof. dr. R.P. Stolk
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Chapter 1

General introduction

PREVALENCE

Of all countries, the USA has the highest prevalence of overweight and obesity. In 2009 - 2010, 32% of the children and adolescents (2-19 years) were overweight or obese (≥85th percentile) and 17% (2-19 years) were obese (≥95th percentile) (1). In the younger children (2-5 years) 27% was overweight or obese (≥85th percentile) and 12% was obese (≥95th percentile). Percentiles were according to Centers for Disease Control and Prevention 2000 growth charts (1). Not only in the US, but also in the rest of the world, the increased prevalence of young children's obesity has become a major issue (1-3). In the Netherlands, the prevalence of overweight and obesity in 2009 was 13-15% in children aged 2-21 years. In children aged 2-5 years the prevalence was 8-18% dependent on age or gender (4).

DEFINITION AND MEASUREMENT OF OBESITY

Obesity is the result of an imbalance between energy intake and energy consumption, causing an excess of fat storage. The non used energy will be stored as fat and a prolonged time of surplus energy will cause obesity. In literature different methods are used to define obesity. The four component-model is used as a reference method for body composition, the model divides the body into fat mass, fat-free water, fat-free protein, and fat-free mineral. Underwater weighting, air-displacement plethysmography, dual energy X-ray absorptiometry (DXA) and total body water, determined by D_2O dilution, are almost as good as the four component-model (r>0.9) (5). Other measures used to provide information on body fatness are skinfold thicknesses and bio electrical impedance analysis (BIA) (5). Because measurements of body fat are time consuming and expensive, proxy measures, like BMI, waist circumference, or waist-to-height ratio are frequently used to define overweight.

BMI is calculated as weight (kg) divided by the squared height (m). In adults, a BMI of 25 or higher and lower than 30 is defined as overweight, and a BMI of 30 or higher is defined as obesity. For children's BMI levels, different classification systems are used to define overweight or obesity. In preschool children, the International Obesity Task Force (IOTF) reference and the WHO standard are used. For the IOTF reference BMI values of 25 and 30 at 18 years of age for boys and girls are linked to child percentiles (6). In table 1 the cut off points for overweight and obesity are shown for children aged 2 to 6 years. The WHO standard is based on age-specific BMI percentiles or standard deviation scores to define overweight and obesity (overweight: +2SDs up to age 5, +1SD thereafter, obesity: +3 SDs to age 5, +2 SDs thereafter) (7). Despite that BMI is a commonly used measure to define overweight and obesity, its reliability is uncertain for this age group, in particular because BMI is not only dependent on fat mass but also on muscle mass.

Table 1. International IOTF BMI cut-offs (kg/m^2) (6)

Age	Boys		Girls	
(years)	BMI 25[1]	BMI 30[1]	BMI 25[1]	BMI 30[1]
2.0	18.36	19.99	18.09	19.81
2.5	18.09	19.73	17.84	19.57
3.0	17.85	19.50	17.64	19.38
3.5	17.66	19.33	17.48	19.25
4.0	17.52	19.23	17.36	19.16
4.5	17.43	19.20	17.27	19.14
5.0	17.39	19.27	17.23	19.20
5.5	17.42	19.46	17.25	19.36
6.0	17.52	19.76	17.33	19.62

[1] indicates BMI percentile corresponding to BMI at age 18 using pooled LMS-based cut-offs. Also available by month of age from 2 to 18 years at http://www.iaso.org/publications/iotfreports/newchildcutoffs/.

ETIOLOGY OF OBESITY

The etiology of obesity is multi-factorial, both different environmental and genetic factors may contribute to the development of obesity in early life. Davison and Birch used an Ecological Systems Theory (EST) to show the complex set of factors from multiple contexts that interact with each other to place a child at risk for overweight (8). In figure 1 the model of Davison & Birch is shown.

HEALTH RELATED CONSEQUENCES OF OBESITY

Childhood obesity has both short term effects (on the obese child) and long term effects (on the adult who was obese during childhood). Short term consequences are increased risk of: psychological or psychiatric problems, in particular low self esteem and behavioral problems; cardiovascular risk factors like high blood pressure, dyslipidemia, abnormalities in left ventricular mass and/or function, abnormalities in endothelial function, and hyperinsulinemia and/or insulin resistance; asthma; low grade systematic inflammation; and orthopedic difficulties (9). Long term consequences are adverse effects on social and economic outcomes in young adulthood, for example, income, educational attainment, and mediated cardiovascular morbidity in adulthood can have its origins in childhood obesity (9).

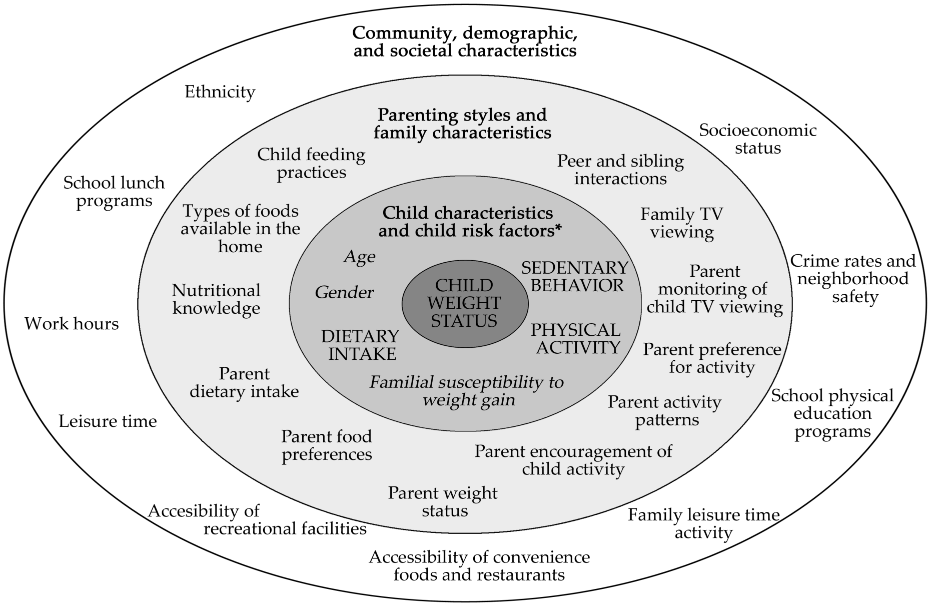

Figure 1. Ecological model of predictors of childhood overweight.
* = Child risk factors (shown in upper case lettering) refer to child behaviors associated with development of overweight. Characteristics of the child (shown in italic lettering) interact with child risk factors and contextual factors to influence the development of overweight (i.e. moderator variables) (From: Davison & Birch 2001(8))

PREVENTION AND TREATMENT OF OBESITY

As discussed before, obesity is caused by a complex set of factors that interact with each other. Therefore, prevention and treatment programs need a multi-factorial design that covers as much risk factors as possible. Available evidence shows that family-based lifestyle interventions with a behavioral program aimed at changing diet and physical activity patterns are able to decrease overweight in both children and adolescents compared to standard care or self-help in the short- and the long-term (10). In preschool children only a small amount of studies investigated the effect of an intervention on obesity. From available studies we know that intervening on obesity at an early age can be effective (11,12) and that intervention at young age may be more effective than intervention later in life (12). To design effective intervention programs, observational studies in young children are needed to gain insight into the determinants of obesity in preschool children. Furthermore, there is evidence that obesity tracks from childhood to adolescence and adulthood (13,14). A large increase in weight between ages 2 to 7 years are associated with adolescent adiposity and metabolic syndrome (15) and overweight and cardiometabolic risk factors in adulthood (16,17). Thus focus on the etiology of overweight in the preschool years (<5 years) is important.

PHYSICAL ACTIVITY

One of the factors related to obesity is physical activity. Physical activity can be defined as any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level. Physical activity is therefore interrelated with energy expenditure; moreover, it may cause an elevation in metabolic rate that persists long after the cessation of observable movement (18). Different methods are available to measure the amount of physical activity in children. More information about these methods can be read in chapter 2. In the past decades accelerometers, small electronic devices to detect movement, are introduced to assess physical activity. Tri axial accelerometers have shown to measure reliably physical activity during the day in adults (19,20) and children (21). Next to total physical activity it can provide information about duration, frequency and intensity of the physical activity, and recently it is found that also the type of activity can be classified (22). Studies investigating the validity of tri axial accelerometers in young children aged 4-6 years are however limited (23,24).

PHYSICAL ACTIVITY GUIDELINES

In preschool children it is unclear how many children achieve the recommended physical activity guidelines. This is caused by several methodological issues.

Firstly, different recommendations on duration and intensity are used in preschool children aged 3 to 5 years old. To begin with, the National Association for Sport and Physical Education (NASPE) recommends to engage in a minimum of 120 minutes of daily physical activity, regardless of the intensity of physical activity, with 60 minutes of structured and 60 minutes of unstructured physical activity. But recent updates to the guidelines state that within these 120 minutes, caregivers should plan opportunities for preschoolers to engage in moderate-to-vigorous physical activity. Therefore the guideline is sometimes interpreted as a minimum of 120 minutes of moderate-to-vigorous physical activity. Also other interpretations of the NASPE guidelines have focused on sufficient physical activity, which is defined as a minimum of 60 minutes of moderate-to-vigorous physical activity daily (25).

Table 2. Actigraph accelerometer cut-off points used to define LPA and MVPA in preschool-aged children

	Age, yr[a]	Age range, yr[b]	LPA, counts per 15 sec	MVPA, counts per 15 sec
Pate et al. (26)	3 – 5	3 – 5	38 - 419	≥ 420
Sirard et al. (27)	3	3 – 5	302 – 614	≥ 615
	4		364 – 811	≥ 812
	5		399 – 890	≥ 891
Reilly et al.; Puyau et al. (28,29)	3 – 4	3 – 4/ 6 - 16	275 – 799	≥ 800
Van Cauwenberghe et al. (30)	5-6	5-6	373 - 584	≥585
Evenson et al. (31)	5-8	5-8	26 - 573	≥574

[a] Age range in which the cut-off points were applied in this sample

[b] Age range in which the original cut-off point validation/ calibration study was conducted.

LPA: Light physical activity, MVPA: Moderate-to-vigorous physical activity

Secondly, different methods are used to measure physical activity, e.g. heart rate monitoring, accelerometers, parental questionnaires etc.; different brands within a method are used (e.g. different brands of accelerometers) and for one specific accelerometer different cut-off points are available in literature. One example is the difference in cut-off points to define light, moderate and vigorous physical activity for the Actigraph, a frequently used uni axial accelerometer (table 2). Beets and colleagues indicated that the interpretation of the guidelines and the differences in cut-off points to define the moderate and vigorous physical activity have a strong impact on the prevalence of preschoolers who engage enough time in health enhancing physical activity (25). In 3 to 5 year old children, mean moderate-to-vigorous physical activity varied from 40 to 269 minutes between the different cut-off points. The percentage of preschoolers that met the guidelines varied from 13.5% to 99.5%, 0.0% to 95.7%, and 0.5% to 99.5% for 120 minutes of total physical activity, 120 minutes of moderate-to-vigorous physical activity, and 60 minutes of moderate-to-vigorous physical activity, respectively (25).

These issues make it difficult to determine the amount of moderate-to-vigorous physical activity and the percentage of children who achieve the recommended amount of health promoting physical activity. In the guidelines and in the cut-off points more uniformity is needed.

ETIOLOGY OF PHYSICAL ACTIVITY

From literature in older children it is known that boys have higher levels of physical activity than girls and that the gender difference is more marked when vigorous activity is considered. The physical activity levels decrease from childhood to young adulthood (18,32). In older children and adolescents, it is found that physical activity is a multidimensional behavior. All factors, personal (biological, psychological and behavioral), social, and physical, contribute the child’s physical activity (33).

Among preschool children (4-6 years), total physical activity is not related to gender and age, but boys do have higher levels of moderate-to-vigorous physical activity. A lower amount of physical activity was associated with family risk of obesity, gestational age and play rules. A higher amount of physical activity was associated with familial interaction in at risk families, parental enjoyment of physical activity, children being the initiator of activities, group compositions. convenient play spaces, frequency in play spaces, rural preschool, active means of transport to school, outdoor variables, weekdays and backyard size was found (34).

The number of studies investigating the etiology of physical activity in preschool children is limited. Most available studies do not use objectively validated measures of physical activity, and most correlates of physical activity have been studied in only one or two studies (34).

HEALTH INCREASING CONSEQUENCES OF PHYSICAL ACTIVITY

Various reviews about the health benefits of physical activity in preschool children found evidence to support a positive relationship between increased or higher physical activity and better measures of adiposity, bone and skeletal health, motor skill development, psychosocial health, cognitive development and aspects of cardiometabolic health (e.g. lipid profile and insulin resistance) (35-37).

It is suggested that investing in physical activity during early years has health benefits later in life, particularly with respect to adiposity (37). Furthermore the development of motor skills is a key factor in the likelihood of participation in various forms of physical activity later in life (38). Finally there is evidence that obesity (13,14), inactivity (39) and physical activity (40) may all track from childhood to adolescence and adulthood, and thus research has to focus on the importance of physical activity in the preschool years (<5 years). Compared to school-aged children and adolescents, in preschool children less is known about the correlates of physical activity and obesity.

GECKO DRENTHE COHORT

Most studies in this thesis are performed within the GECKO Drenthe cohort. GECKO Drenthe is a birth cohort within the Groningen Expert Center for Kids with Obesity (GECKO) and has been designed to assess risk factors for childhood obesity. The cohort included almost 3000 children born in a 1-year period in Drenthe, the Netherlands. Mothers who gave birth between April 1st 2006 and April 1st 2007 were included in the study (41). Some additional children, born till February 2008, were also included, because they participated in an intervention study, also part of GECKO. All children will be followed from pregnancy of their mother till adulthood. Genetic, biomedical, social, environmental, physical activity and dietary data of the children and their parents will be collected.

During pregnancy parents filled in a questionnaire about reproductive/ medical history, social structures, lifestyle, diet and smoking. After delivery, tissue and blood of the umbilical cord was collected and the placenta was weighted, further clinical data concerning the pregnancy and delivery was collected by the midwives, obstetricians and general practitioners. Till the age of 4 years, children visited Well Baby Clinics for 14 times. Height, weight, head circumference (till 11 months), waist circumference and hip circumference were measured by trained nurses. During those visits parents filled in a questionnaire about diet, physical activity, development, social structures and parenting. Bioelectrical impedance analysis and ultrasound measurements were done at 2 and 7 months of age in a small group of children and HbA1c was measured at 9 months of age in another small group of children. In all children blood serum was collected at 9 months of age, urine and blood pressure at the age of 2 years and physical activity was measured between 3 and 6 years of age. Around the 5th birthday children were measured by the municipal health service in their 2th year of preschool. Height, weight, waist circumference and blood pressure were measured. After the measurement an invitation for an online questionnaire was send to the parents. In table 3, a detailed scheme of all available data and materials is shown.

Table 3. Data collection GECKO Drenthe birth cohort

Age (months)	**0**	**0.5**	**1**	**2**	**3**	**4**	**6**	**7**	**9**	**11**	**14**	**18**	**24**	**36**	**45**	**60**
Instance																
Well Baby Clinics		x	x	x	x	x	x	x	x	x	x	x	x	x	x	
Youth Health Services																x
QUESTIONNAIRES																
Questionnaire	1[a]	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Dietary intake		x	x	x	x	x	x	x	x	x	x	x	x		x	x
FFQ														x	(x)	
PA parents	x				x										x	(x)
PA/ sedentary child									x	x	x	x	x		x	x
Health	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x
Behavior		x	x	x	x	x	x		x			x	x		x	x
Environment	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SDQ																x
MEASUREMENTS																
Length / height			x	x	x	x	x	x	x	x	x	x	x	x	x	x
Body weight			x	x	x	x	x	x	x	x	x	x	x	x	x	x
Head circumference			x	x	x	x	x	x	x	x						
Waist circumference			x	x	x	x	x	x	x	x	x	x	x	x	x	x
Hip circumference			x	x	x	x	x	x	x	x	x	x	x	x	x	
Blood pressure, pulse													x			x
Movement sensor														x	x	x
BIA (subgroup)				x				x								
Ultrasound (subgroup)				x				x								
HbA1c (subgroup)									x							
BIOMATERIALS																
Cord blood (storage)	x															
Cord tissue (storage)	x															
Blood sample (storage)									x							
Urine (only analysis)													x			

[a] 3 parts: father, mother, and delivery characteristics

FFQ: food frequency questionnaire, PA: physical activity, SDQ: Strengths and difficulties questionnaire (social behavior)

OBJECTIVES AND OUTLINE OF THIS THESIS

The first objective is to validate and evaluate methods used to assess overweight, energy used for maintenance and growth, and energy used for physical activity in preschool children. The second objective is to examine correlates of physical activity, sedentary behavior and overweight in preschool children.

The first part of this thesis, partly chapter 2 and chapters 3 to 5, focuses on methodological issues in the measurement of obesity and physical activity. In **chapter 2** a review is performed to summarize existing literature on the association between directly assessed physical activity and adiposity in preschool children (age 1.5 to 6 years). Differences between measures of physical activity and adiposity are discussed. In **chapter 3** it is assessed whether waist-to-height ratio is a better estimate of body fat percentage and cardiometabolic risk factors than BMI or waist circumference in children aged 3 to 7 years old. In **chapter 4** energy requirements for maintenance and growth, measured by indirect calorimetry was compared against existing equations predicting these requirements in 3 to 4 year old children. In **chapter 5** the validity evidence of the TracmorD to determine energy used for physical activity was assessed in 3 to 4 year old children.

To prevent overweight in adolescence and adulthood, detection and treatment of overweight and obesity already in the first years of life are necessary. Physical activity or sedentary behavior of children during the first years of life might influence its activity level and thereby influence growth in early childhood. In **chapter 2** and in **chapters 6 to 8**, the association of physical activity or sedentary behavior with overweight in preschool children is assessed. In **chapter 6** it is examined whether the time that an infant is able to move unrestrictedly and time spent in baby seats are related to weight and waist circumference at age 9 months and growth from 9 to 24 months. In **chapter 7** the interplay between screen time, sleep duration, outdoor play, having a TV in the bedroom and the number of TVs at home and their association with BMI in 3 to 4 year old children is investigated. In **chapter 8** it is examined whether parental physical activity and BMI are associated with physical activity, BMI and waist circumference in children aged 2 to 5 years old.

In **chapter 9** a general discussion of the findings and some future perspectives are provided.

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Chapter 2

Is directly measured physical activity related to adiposity in preschool children

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International Journal of Pediatric Obesity 2011; 6:389-400

ABSTRACT

This review summarizes the association between directly assessed physical activity and adiposity in preschool children (age 1.5-6 years). It includes 17 cross-sectional and longitudinal studies that were published between January 1999 and February 2010. The association between physical activity and obesity seems to depend on the outcome measure of adiposity. In 60% (3/5) of the studies using percentage body fat an inverse significant relationship with physical activity is found against 18% (2/11) of the studies that used body mass index as method to assess adiposity. Physical activity is inversely related to percentage body fat in preschool children. The associations between physical activity and body mass index as a measure of adiposity in preschool children remain elusive. Further studies using directly measured physical activity and percentage body fat to define adiposity are needed to draw more firm conclusions.

INTRODUCTION

Obesity is a growing epidemic worldwide, not only in adults but also in children (1,2). From the perspective of prevention, the findings in very young children are of particular relevance. The global prevalence of overweight and obesity is estimated to be 6.7% in very young children of age 0-5 years of age. In developed countries, overweight and obesity are currently more common in this young age group, leading to an estimate of 11.7% in developed countries (3). Similar as in adults, children with overweight or obesity have a substantially increased health risk (4-6). This applies to metabolic impairments such as hypertension, hyperinsulinaemia, poor glucose tolerance and a raised risk for type 2 diabetes. In addition to metabolic impairments, psychological (anxiety, depression or low self esteem) and social consequences (peer rejection) are important in children with obesity (4). Furthermore, it is known that children with overweight or obesity have a high chance to be obese in adulthood (7-10). An important difference between children and adults is that children experience growth, and not only current weight is a risk factor for future overweight, but also the increase in body mass index (BMI) over a certain period of time. Studies have found that BMI change between the age of 2 and 6 is related to overweight and cardio metabolic risk in adulthood (11,12). For prevention of obesity and related comorbidities in adulthood it is therefore important to prevent overweight and obesity early in life.

Obesity is the result of a disturbed balance between energy intake and energy expenditure. Physical activity is therefore an important factor related to overweight and obesity in adults (13), and recent reports on children ranging in age from 2-18 years show that this is also relevant during growth and development at younger age (14,15). In addition, physical activity may track from childhood into adulthood (16). In the preschool period, physical activity may have a protective effect because of the ‘adiposity rebound’. The onset of the second period of rapid growth in BMI, the adiposity rebound, starts at about age six (17,18). An early adiposity rebound is associated with adult obesity (19). High levels of physical activity may delay the onset of the adiposity rebound. Therefore, the level of physical activity before the age of 6, the preschool age, might play a pivotal role in the development of obesity in adulthood (20).

Little is known about the association between physical activity and adiposity in preschool children, mainly due to methodological issues (21). However, a recent increase in studies using objective devices such as accelerometers to assess physical activity is seen and advances in accelerometry and automated data processing. Physical activity can be defined as any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level. To assess physical activity, an instrument must be sensitive enough to detect all activities that are executed by the child. Some methods are only able to assess total physical activity, while others are also able to assess differences in frequency, duration and intensity of physical activity. To assess physical activity in children, indirect subjective measures can be used, such as parent/teacher questionnaires and parental recall (22,23). The disadvantage of these measurements is that teacher or parent questionnaires have not been sufficiently evaluated for the assessment of physical activity in preschool children (23). This can be caused by the sporadic nature of movement behaviour in preschoolers. Self report, also a subjective measure, is not recommended for children under age 10 (24). Alternatives that have been developed in the past years are direct methods such as accelerometers and pedometers, whereas the more traditional validated methods include the double labelled water (DLW) method, heart rate monitoring and direct observation (23,25). An increased amount of studies arise using accelerometers to assess physical activity. Accelerometers are validated objective measures to assess physical activity in preschool children (26). Some of these studies investigated whether a lack of physical activity in children below 6 years is already related to adiposity, but the results appear inconsistent. The aim of this review is to summarize findings on the association between physical activity, assessed by direct methods and adiposity in preschool children aged 1.5-6 years.

METHODS

Search procedures

Relevant studies were identified through searches of Pubmed, Embase, Medline and Web of Science with the following keywords: (children or preschool or 'young children') and ('body mass index' or BMI or overweight or obesity or 'body fat' or 'body composition' or 'weight status') and ('physical activity' or 'activity level' or exercise). The reference lists of the identified studies including reviews were searched until no further studies were identified. A summary of the characteristics of the studies relevant for this review were composed in Table 1.

Inclusion and exclusion criteria

The inclusion criteria were (i) physical activity measured with direct methods (accelerometer, pedometer, DLW method, heart rate monitoring or direct observation), (ii) adiposity measured as BMI, percentage body fat (%BF) or fat mass (FM) as outcome measure, (iii) the association between physical activity and adiposity was investigated, (iv) children in the study were aged 1.5- 6 years at baseline, (v) the study was published between January 1999 and February 2010, and (vi) the study had a cross-sectional or longitudinal design. The exclusion criteria were (i) the study contained children with disabilities, (ii) the study was not published in English, and (iii) anthropometric measures reported by the parents. No criteria were applied for study size, ethnicity, gender distribution or duration of physical activity measurement.

Analysis

A quantitative meta-analysis was not possible due to lack of studies and heterogeneity with regard to methods to assess physical activity or adiposity. Therefore this review aims to give a complete descriptive overview of previous findings relating to the topic, confined to studies that assess daily physical activity using direct methods. The authors who did not present correlation coefficients and p-values were contacted to obtain this information. The results of the authors who responded were added in Table 1.

The included studies were stratified by outcome measure for adiposity. The relation of physical activity with %BF, FM and BMI were described separately and gender differences were analysed if possible. To summarize the consistency of evidence a scheme proposed by Sallis et al. (27) was used; 0-33% of studies supporting the association stand for no association, 34-59% stands for a inconsistent association and 60-100% stands for a positive or negative association (27).

RESULTS

Study selection

A flow diagram for the selection of studies is provided in Figure 1. Sixty studies were identified based on the title and abstract, of which 17 articles fitted the inclusion criteria. Participants' age, sample size, percentage boys and girls, countries where the studies were conducted, methods to assess physical activity and adiposity, statistical analysis and results are presented in Table 1. In short, physical activity was mostly measured using accelerometers (28-38), but also using pedometers (39), heart rate monitoring (40), DLW method (41) and direct observation (36,42,43). Adiposity was measured with BMI, %BF or FM as outcome measures. %BF and FM were assessed by DXA, skin fold measurement and ^{18}O dilution method. The participants' age ranged from 1.5-7 years. Study size ranged from 44– 438 participants. The studies were conducted in The USA, Europe, Asia and Australia.

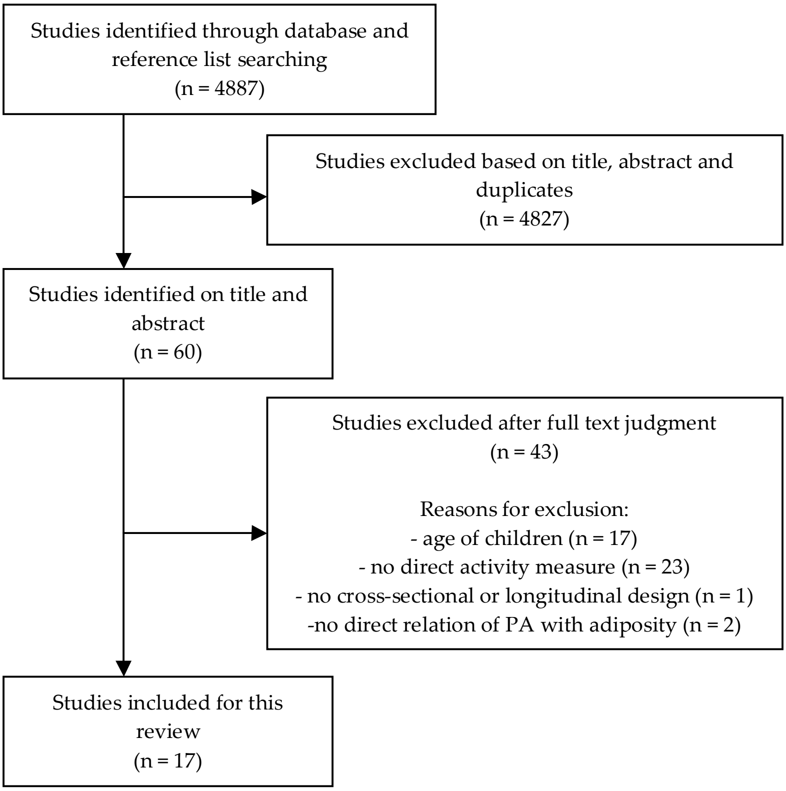

Figure 1. Flow diagram of the literature review strategy

The relation between physical activity and adiposity

Of all included studies, 29% (5/17) found an inverse relationship between physical activity and adiposity (34-37,41). One study found this relationship in boys, but not in girls (36); 12% (2/17) found a positive relationship between physical activity and adiposity (32,42); 59% (10/17) found no relationship between physical activity and adiposity (28-31,33,38-40,43,44). Since the inconsistency of the findings may be due to the methodology used to assess adiposity, the results are split by outcome measure of adiposity in the next sections.

Physical activity and percentage body fat

Of the eligible studies, 29% (5/17) used %BF to express adiposity (28,35,37,39,41). Sixty percent (3/5) of these found a significant inverse relationship between physical activity and %BF (35,37,41). Of those that found a significant relationship, two studied this relation cross-sectionally (35,41) and one studied this relation longitudinally (37). The other 40% (2/5) found a non-significant but inverse relationship between physical activity and %BF (28,39).

Physical activity and BMI

Of the eligible studies, 65% (11/17) used BMI and/or BMI Z-score to express adiposity (28,30-34,36,36,38,40,42,44). Eighteen percent (2/11) of these found a significant inverse relationship (34,36). One of these two significant studies measured physical activity only during preschool hours and found this relationship only in boys, but not in girls (36). Sixty-four percent (7/11) found no significant relationship between BMI and/or BMI Z-score and physical activity (28,30,31,33,38,40,44). Eighteen percent (2/11) found a positive significant relationship between BMI Z-score and physical activity (32,42). When taking BMI or BMI Z-score as a measure for adiposity, no association was found between physical activity and adiposity.

Physical activity and fat mass

Of the eligible studies, 24% (4/17) calculated the relation between physical activity and FM (28,29,35,43). Twenty five percent (1/4) of them found an inversely significant relationship of total and vigorous physical activity with FM (35); 75% (3/4) found no significant relationship between physical activity and FM (28,29).

Gender differences

Only three out of 17 studies analyzed the relation between physical activity and %BF (35) or BMI (28,36) for boys and girls separately. Janz et al. found a similar significant inverse relationship of physical activity with %BF and FM for boys and girls (35). Trost et al. found that overweight boys were significantly less physically active compared to non-overweight boys, whereas in girls they found no differences (36). Heelan and Eisenmann found no relation between physical activity and BMI for both boys and girls (28).

DISCUSSION

In contrast to the studies that used BMI as the outcome measure for adiposity, most studies (60%) that used %BF as outcome measure for adiposity found evidence for an inverse relationship between physical activity and adiposity in preschool children.

Physical activity and percentage body fat

According to the scheme proposed by Sallis et al. (27) there is enough evidence to state that there is an inverse association between %BF and physical activity. This is supported by the finding that the other 40% found inverse associations as well, although not significant. One (39) of the two studies that did not find a significant relationship used pedometers instead of accelerometers to assess physical activity. Pedometers may be less accurate than accelerometers in preschool children because they only detect the number of steps and not the intensity of vertical acceleration like in accelerometers (23). Furthermore, the daily physical activity of preschool children consists partly of walking but includes many other movements as well.

With regard to the type of physical activity, it has been suggested that vigorous physical activity may have a larger effect on adiposity in children than milder forms of activity (45). The participants in the cross-sectional study of Janz et al. (35) are the same as the baseline participants of the longitudinal study of Janz et al. (37). They found in their cross-sectional analysis that in contrast to moderate physical activity, vigorous physical activity was related to the %BF. In addition in the longitudinal study this effect was also found in the relation with vigorous physical activity when the rate of change in %BF between baseline and follow up was used. This is in line with studies in older children and adolescents that found that after adjustment for demographic factors, vigorous physical activity contributed to a lower %BF. For moderate physical activity this effect was not found (46,47).

The relationship between objectively measured physical activity and adiposity has been reviewed to a limited extend before by Jimenez-Pavon et al. (21). Due to the low number of studies in preschool children, they were not able to distinguish between the use of %BF or BMI in their analysis. In preschool children they found in three out of five studies a significant inverse relationship between physical activity and adiposity (21). In the total age group (age 0-18) they distinguished between adiposity measures. In 81% (25/31) of the studies that used simple proxies of adiposity as outcome measure (e.g. BMI), and in 76% (13/17) of the studies that used more precise body composition methods (e.g. DXA, skin folds and impedance) a significant inverse relationship between habitual physical activity and adiposity was found (21). Hawkins and Law (48) reviewed the relation between physical activity and adiposity in preschool children using studies that report on physical activity assessed by direct measurement of energy expenditure, observation or parental report. Only 41% reported an inverse relationship. This can be caused by the inclusion of studies using parental report to assess physical activity (48).

Physical activity and BMI

The studies that used BMI and/or BMI Z-score to express adiposity showed no relationship between physical activity and adiposity. In children, BMI is commonly used as an easy measure to identify adiposity. Cole *et al.* provided age and sex specific cut off points for BMI in children that correspond to the adult cut off points of 25.0-29.9 kg/m^2 for overweight and above 30 kg/m^2 for obesity (49). These reference curves have become known as the International Obesity Taskforce standards (50). Another method to define overweight and obesity is by using percentiles. A BMI percentile from the 85th to 95th percentile may be defined as overweight and a BMI above the 95th percentile is defined as obesity (e.g. Centers for Disease Control and Prevention (CDC) 2000 growth charts) (50). In addition to BMI, BMI Z-scores (BMI SD scores) are used to evaluate a child's BMI in terms of standard deviations from the mean for children of the same age and gender. In children below 2 years of age, the weight-for-length percentiles are used to evaluate weight relative to linear growth. Weight-for-length above the 95th percentile in these children is defined as overweight (50). Despite that BMI is a commonly used measure to define overweight and obesity, its reliability is uncertain for this age group, in particular because BMI is not only dependent on fat mass but also on muscle mass. In relatively fat children, BMI can be a good indicator of excess adiposity. However, in children classified as overweight, a high BMI is more often explained by relatively large muscle mass (51,52) leading to frequents misclassification. Since more children in the included studies were overweight rather than obese, it is possible that misclassification for mild excess adiposity obscured the relation between BMI and physical activity. %BF may therefore be more useful to identify children with mild excess adiposity classified as overweight (53). The possibility for the use of waist circumference in this young age group should be explored as well for the future (54,55).

Physical activity and fat mass

The relationship between physical activity and fat mass (FM) is not clear from the published studies. The disadvantage of FM is that it is an absolute value. Since it does not take into account total body size, a large fat mass may be accompanied by a large muscle mass, which confounds the outcomes, especially for determinants like physical activity that are partly dependent on muscle mass. %BF is a better method, because it better reflects the body proportions.

Gender differences

Is there a difference in the relation of physical activity with adiposity between boys and girls? It is often found that preschool boys are more active than preschool girls (56), and girls have more body fat than boys (29,35,39). Of the three studies included in this review that analyzed the relation between physical activity and %BF (35) or BMI (28,36) for boys and girls separately, only one (36) found that overweight boys were significantly less physically active compared to non-overweight boys, whereas in girls they found no differences. This study measured physical activity only during preschool hours. As explanation the overall low activity levels in girls (floor effect) is suggested (36). An alternative explanation given is related to reverse causation, i.e. that boys engage in more vigorous-intensity activities, play in larger groups in more open settings, engage in more risk-taking behaviour, and play rougher games involving greater amounts of body contact than girls (36). These types of activities may be more influenced by excess adiposity.

Methods to assess physical activity

When studying the relation between adiposity and physical activity, the challenge is to define both aspects as accurate as possible. Most of the included studies in this review used accelerometers to assess physical activity. Accelerometers measure time-varying differences in force or accelerations. They are able to assess total physical activity and differences in frequency, duration and intensity of physical activity (57). Accelerometers are small and lightweight and have been calibrated and validated in children (26,58-60). Most of the accelerometers in this review were uni axial, measuring accelerations only in the vertical plane, to assess physical activity. In school-aged children there is no evidence that tri-axial or omni directional accelerometers are more reliable than uni axial accelerometers (61). In preschoolers limited research has been carried out into the difference in capturing physical activity with either uni axial or tri-axial accelerometers (62). It is possible that tri-axial accelerometers could be better at capturing total children's activity in young children since they tend to move in more directions at the same time than older children and adults (23). For example the walking pattern in young children contains more horizontal components, because of a bigger step width (63). Tri-axial accelerometers seem to have a good reproducibility and a good validity, but there is limited information about the reproducibility and validity of tri-axial accelerometers in preschool children (61). We did not find studies using tri-axial accelerometers to assess the relation between physical activity and adiposity in preschool children.

Other methods used in the included studies in addition to accelerometers and pedometers were heart rate monitoring, PAL calculated from the DLW method and direct observation. Heart rate monitoring provides information about total energy expenditure and about the amount of time spent in high-intensity activity. It is a relatively cheap method to assess physical activity, but less feasible to use in preschool children. Another disadvantage is that heart rate is also affected by other factors than physical activity, such as emotional stress and high ambient temperature (64). The DLW method does not directly measure activity but is a valid and reliable measure for total energy expenditure in adults and children (65). After intake of double labelled water ($^{2}H_2{}^{18}O$), the ^{18}O is lost in body water and carbon dioxide, whereas ^{2}H is lost only in body water. The energy expenditure can be calculated from the decays of ^{2}H and ^{18}O enrichment in body water, easily sampled as urine or saliva. Total energy expenditure can be used to calculate the physical activity level if the basal metabolic rate is assessed (66,67). In direct observation a researcher watches the subject and directly records physical activity. It assesses detailed information on children's physical activity patterns and types in variety of settings, including the ability to measure upper body movement. A disadvantage is the time consuming and thus expensive data collection, so direct observation is less feasible for large-scale studies, or for individual data collections over extended periods of time (23). We expect that, in contrast with the issues on methodology to assess adiposity, the different direct methods to assess physical activity should all find a result in the same direction, despite the differences regarding their interpretation.

Longitudinal versus cross-sectional studies

From the cross-sectional studies in this review no definitive conclusion can be made about causal relationships. Two longitudinal studies were found on the relation between physical activity and adiposity measures. Only one study used %BF as measure for adiposity. They found an inverse relation between vigorous physical activity at baseline with the rate of change in %BF between baseline and follow up (37). The other longitudinal study found no relation between physical activity, measured between 15.00 and 18.00 h, and the sum of 7 skinfolds in mm as indicative measure for fat mass (43). In a review focused on the longitudinal association between physical activity and adiposity in adolescence, most studies showed protective effects of physical activity against adiposity, mainly in the participants who were already obese at baseline (68). Some studies in older children, adolescents and adults found no prospective association between physical activity and the development of adiposity (69). More longitudinal research on the predictive effect of physical activity of preschoolers on childhood obesity is necessary.

Strengths and limitations

As opposed to previous reviews, in this review it was possible to distinguish between studies using %BF or BMI in their analysis, with important consequences for the conclusion. A limitation is the low availability of longitudinal studies. Most studies in this review are cross-sectional and no definitive conclusions on cause and effect can be drawn. However these results indicate that longitudinal and intervention studies are needed and indicated. Another limitation is that relevant studies may have been missed due to publication bias or because they were not published in English.

CONCLUSION

The present evidence suggests that physical activity is inversely related to %BF at very young age. The associations between physical activity and BMI as a measure of adiposity in preschool children remain elusive. Further studies using direct methods to measure physical activity and using %BF to define adiposity are needed to draw firm conclusions.

Table 1. Studies on the association between physical activity, assessed by direct methods, and adiposity in preschool children

Author (publication year)	*Methods to assess PA*	*Methods to assess adiposity*	*Study subjects*	*Statistical analysis and results*
Studies using %BF and/or FM to assess adiposity				
Al-Hazzaa & Al-Rasheedi (2007) (39)	Pedometer (Step counts per day)	%BF (triceps and sub-scapular skin fold measurements) Obesity is defined as: - Boys: ≥ 25 %BF, - Girls ≥ 30 %BF	n = 224 Age: 3.4-6.4 yr Location: Jeddah, Saudi Arabia	Independent t-test Obese: 5375 ±3754 steps/day Non-obese: 7065 ±5495 steps/day p: 0.109 Pearson correlation Steps/day - %BF r: 0.078; p: 0.27
Janz *et al.* (2002) (35)	Uni-axial accelerometer (Total PA (average counts/min); MVPA (min/day); VPA (min/day))	%BF, FM and trunk FM (DXA)	n = 434 Age: 4-6 yr Location: Iowa, USA	Pearson correlation *Total PA - %BF* boys: r: -0.19; p<0.01*; girls r: -0.25; p<0,01* *Total PA - FM* boys: r: -0.15 p<0.05*; girls: r: -0.19; p<0.01* *MPA - %BF* boys: r: -0.10 p>0.05; girls: r: -0.12; p>0.05 *MPA – FM* boys: r: -0.07 p>0.05; girls: r: -0.06; p>0.05 *VPA - %BF* boys: r: -0.26; p<0.01*; girls: r: -0.30; p<0,01* *VPA - FM* boys: r: -0.22; p<0.01*; girls: r: -0.25; p<0,01*
Janz et al. (2005) (37)[a]	Accelerometer (average counts/min; VPA (min/day) MPA (min/day); 5 min bouts VPA, MPA)	%BF (DXA)	N=379 Age at baseline: 5.6 ± 0.5 yr Age at follow up: 8.6 ± 0.5 yr Location: Iowa, USA	Wilcoxon rank sum test *Average counts/min - quartiles of follow up %BF* lower quartile: 748; upper 3 quartiles: 700; p<.05* lower 3 quartiles: 725; upper quartile: 670; p<.005* *VPA - quartiles of follow up %BF* Lower quartile: 32; upper 3 quartiles: 27; p<.005* lower 3 quartiles: 30; upper quartile: 24; p<.005* *MPA - quartiles of follow up %BF* Lower quartile: 217; upper 3 quartiles: 213; p>.05 lower 3 quartiles: 215; upper quartile: 211; p>.05 *5 min bouts VPA - quartiles of follow up %BF* Lower quartile: 1.3; upper 3 quartiles: 1.0; p<.05* lower 3 quartiles: 1.1; upper quartile: 0.7; p<.005* *5 min bouts MPA - quartiles of follow up %BF* Lower quartile: 22; upper 3 quartiles: 21; p>0.05 lower 3 quartiles: 22; upper quartile: 20; p>.005

Table 1. (continued)

Author (publication year)	*Methods to assess PA*	*Methods to assess adiposity*	*Study subjects*	*Statistical analysis and results*
Heelan & Eisenmann (2006) (28)	Uni-axial accelerometer (total PA (average counts/min); MPA (min/day); MVPA (min/d); VPA (min/day))	%BF and FM (DXA) BMI	n = 100 Age: 4-7 yr Location: a rural Midwestern US community (population: 30,000)	Partial correlation coefficients adjusting for chronological age *TPA – BMI* boys: r: -0.17; p>0.05; girls: r: -0.10; p>0,05 *TPA - %BF* boys: r: -0.06; p>0.05; girls: r: -0.08; p>0,05 *TPA – FM* boys: r: -0.13; p>0.05; girls: r: -0.08; p>0,05 *MVPA – BMI* boys: r: -0.25; p>0.05; girls: r: 0.04; p>0,05 *MVPA - %BF* boys: r: -0.12; p>0.05; girls: r: -0.09; p>0,05 *MVPA – FM* boys: r: -0.22; p>0.05; girls: r: -0.08; p>0,05
Jackson *et al.* (2009) (29)	Uni-axial accelerometer (average counts/min)	FM (DXA)	n = 89 Age: 2–6 yr Location: Scotland, UK	GLM analysis with average PA as a dependent variable. FM was no predictor of PA, F: unknown; p: 0.617
Atkin & Davies (2000) (41)	DLW method (TEE) BMR PAL: TEE/BMR	%BF (^{18}O dilution method)	n = 77 Age: 1.5-4.5 yr Location: Great Britain, UK	Multiple regression analysis with dietary intake variables and PAL as predictors of %BF *PAL - %BF* Coefficient: -8.18; t ratio: -3.45; p<0.001*
Robertson et al. (1999) (43)[a]	Children's Activity Rating Scale (CARS); only in time interval 3 PM to 6 PM.	FM (sum of 7 skinfolds)	Take-off group: n=14 Control group: non-take-off group n = 30 Age: 3-7 yr Location: Texas, USA	Mixed models ANOVA PA measured in 1 year before take-off *Average PA (mean CARS score)- take-off/non-take-off* Take-off: 2.0 ±0.2 non-take-off: 2.0 ±0.2; p = 0.77 *MVPA (%min)- take-off/non-take-off* Take-off: 33.7 ±14.5 non-take-off: 27.0 ±19.3; p = 0.30 *VPA (%min)- take-off/non-take-off* Take-off: 1.5 ±1.7 non-take-off: 1.2 ±1.8; p = 0.70
Studies using BMI and/or BMI Z-score to asses adiposity				
Finn *et al.* (2002) (30)	Bi-axial accelerometer (average daily counts; counts between 9 AM and 5 PM; % time spent in VPA)	BMI	n = 214 Age: 3-5 yr Location: South Dakota, USA	Forward-backward stepwise regression analysis *average daily counts –BMI* partial r^2: unknown; p: 0.4 *counts between 9 AM and 5 PM – BMI* partial r^2: unknown; p: 0.9 *%time VPA - BMI* partial r^2: unknown; p: 0.3

Table 1. (continued)

Author (publication year)	*Methods to assess PA*	*Methods to assess adiposity*	*Study subjects*	*Statistical analysis and results*
Firrincieli *et al.* (2005) (31)	Omni directional accelerometer (average counts/min; amount VPA; amount sustained VPA)	BMI	n = 54 Age: 3-5 yr Location: Richmond, Virginia, USA	Correlation *PA - BMI* r: unknown; p>0,05
Jackson *et al.* (2003) (32)	Uni-axial accelerometer (average counts/min)	BMI BMI Z-score	n = 104 (60) Age: 3-4 yr Location: Scotland, UK	Correlation *PA – BMI Z-score* r: 0.19; p: 0.04*
Jones et al. (2009) (38)	Uni-axial accelerometer (average count/min; MVPA (min/day)	BMI NOW and OW was classified based on the IOTF reference for children	n = 58 Age: 2-6 yr Location: New South Wales, Australia	Independent t-test *Average counts/min - BMI* OW: 961.08 ± 213.05 counts/min NOW: 865.71 ± 226.18 counts/min p: 0.297 *MVPA* OW: 28.99 ± 22.55 min/day NOW: 32.95 ± 25.24 min/day p: 0.696
Kelly *et al*. (2006) (33)	Uni-axial accelerometer (average counts/min)	BMI BMI Z-score	n = 339 Age: 4.2± 0.5 yr Location: Scotland, UK	Univariate analysis *PA – BMI Z-score* Coefficient: 17.4; p: >0.05
Metallinos-Katsaras *et al.* (2007) (34)	Uni-axial accelerometer (Light PA (min/day); MPA (min/day); VPA (min/day); very VPA (min/day); active time (min/day); very active time (min/day); TPA (average counts/min)	BMI BMI Z-score OW is defined as: BMI Z-score ≥85th percentile according to the CDC Growth Charts	n = 56 Age: 2-5 yr Location: Massachusetts, USA	Logistic regression analysis Adjusted for age, race and sex 2 groups: NOW and OW children *Light PA – NOW /OW* Adjusted odds ratio (95% CI): 1.00 (0.99 to 1.01); p: 0.36 *MPA - NOW /OW* Adjusted odds ratio (95% CI): 1.00 (0.99 to 1.02); p: 0.97 *VPA - NOW /OW* Adjusted odds ratio (95% CI): 0.94 (0.88 to 0.99); p<0.05* *Very VPA - NOW /OW* Adjusted odds ratio (95% CI): 0.68 (0.48 to 0.96); p: 0.03* *MPA - NOW /OW* Adjusted odds ratio (95% CI): 1.00 (0.99 to 1.02); p: 0.97 *Active time – NOW /OW* Adjusted odds ratio (95% CI): 1.00 (0.98 to 1.01); p: 0.54 *Very active time - NOW /OW* Adjusted odds ratio (95% CI): 0.94 (0.89 to 0.997); p: 0.04* *TPA - NOW /OW* Adjusted odds ratio (95% CI): 1.00 (0.99 to 1.00); p: 0.43

Table 1. (continued)

Author (publication year)	***Methods to assess PA***	***Methods to assess adiposity***	***Study subjects***	***Statistical analysis and results***
Toschke *et al.* (2007) (44)	Uni-axial accelerometer (average counts/min)	BMI	n = 192 Age: 5-6 yr Location: Munich, Germany	Pearson correlation *PA – BMI* r = -0.06; p>0.05
Trost *et al.* (2003) (36)	Uni-axial accelerometer (total counts/hour; number 15s-intervals of MVPA; number 15s-intervals of VPA); only during preschool hours Observational System for Recording Physical Activity in Children- Preschool version (OSRAC-P); only 1 hour/day (mean activity rating)	BMI Overweight is defined as: BMI ≥85th percentile according to the CDC Growth Charts	N = 245 Age: 3-5 yr Location: Columbia, South Carolina, USA	Two-way ANCOVA with sex and OW or NOW as grouping variables, parent education as covariate *TPA - NOW /OW* boys, OW: 50.5 $x10^3$; NOW: 60.0 $x10^3$; p<0.05* girls, OW: 51.9 $x10^3$; NOW: 52.1 $x10^3$; p>0.05 *% time MVPA- NOW /OW* boys, OW: 39.0; NOW: 47.6; p<0.05* girls, OW: 42.2; NOW: 41.6; p>0.05 *MVPA intervals - NOW /OW* boys, OW: 27.2; NOW: 33.7; p<0.05* girls, OW: 28.3; NOW: 28.5; p>0.05 *VPA intervals- NOW /OW* boys, OW: 4.9; NOW: 6.7; p<0.05* girls, OW: 4.7; NOW: 5.6; p>0.05 *mean activity rating- NOW/OW* boys, OW 2.4; NOW: 2.6, p<0.05* girls, OW 2.5; NOW: 2.5, p>0.05
Jago *et al.* (2005) (40)	HR monitoring: HR PA/h (min/hour with mean HR of >140bpm)	BMI	n = 142 in year 1 n = 141 in year 2 n = 137 in year 3 Age: 3-6 yr Location: Texas, USA	Pearson correlation *HR PA/h –BMI* yr 1, r: 0.105; p>0.05 yr 2, r: 0.027; p>0.05 yr 3, r: 0.027; p>0.05
Pate et al. (2008) (42)	Observational System for Recording Physical Activity in Children- Preschool version (OSRAC-P); only during preschool hours	BMI	n = 438 Age: 3-5 yr Location: Colombia, South Carolina, USA	Multiple regression analysis with gender, age, BMI, race and preschool as predictors of % time active and of % time MVPA % time active - BMI (age 3-5) Beta: .17; F: 15.41; p <.001* % time MVPA – BMI (age 4-5) Beta: .14; F: 9.08; p.003*

%BF, percentage body fat; BMI, body mass index; BMR, basal metabolic rate; bpm, beats per minute; CDC, Centers for Disease Control and Prevention; CI, confidence interval; DLW, double labelled water; DXA, dual energy X-ray absorptiometry; FM, fat mass; HR, heart rate; IOTF, International Obesity Taskforce; min, minutes; MPA, moderate physical activity; MVPA, moderate-to-vigorous physical activity; NOW, non overweight; OW, overweight; PA, physical activity; PAL, physical activity level; TEE, total energy expenditure; TPA, total physical activity; UK, United Kingdom; USA, United States of America; VPA, vigorous physical activity; yr, year * p < 0.05

[a] A longitudinal design instead of a cross-sectional design in the other studies.

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Chapter 3

Waist-to-height ratio, waist circumference and BMI as indicators of percentage fat mass and cardiometabolic risk factors in children aged 3 to 7 years

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Clinical Nutrition 2013, in press

ABSTRACT

OBJECTIVE. To assess whether waist-to-height-ratio (WHtR) is a better estimate of body fat percentage (BF%) and a better indicator of cardiometabolic risk factors than BMI or waist circumference (WC) in young children.
METHODS. WHtR, WC and BMI were measured by trained staff according to standardized procedures. ^2H_2O and $^2H_2{}^{18}O$ isotope dilution were used to assess BF% in 61 children (3-7 years) from the general population, and bio-electrical impedance (Horlick equation) was used to assess BF% in 75 overweight/obese children (3-5 years). Cardiometabolic risk factors, including diastolic and systolic blood pressure, HOMA2-IR, leptin, adiponectin, triglycerides, total cholesterol, HDL- and LDL-cholesterol, TNFα and IL-6 were determined in the overweight/obese children.
RESULTS. In the children from the general population, after adjustments for age and gender, BMI had the highest explained variance for BF% compared to WC and WHtR (R^2=0.32, 0.31 and 0.23, respectively). In the overweight/obese children, BMI and WC had a higher explained variance for BF% compared to WHtR (R^2=0.68, 0.70 and 0.50, respectively). In the overweight/obese children, WHtR, WC and BMI were all significantly positively correlated with systolic blood pressure (r=0.23, 0.30, 0.36, respectively), HOMA2-IR (r=0.53, 0.62, 0.63, respectively), leptin (r=0.70, 0.77, 0.78, respectively) and triglycerides (r=0.33, 0.36, 0.24, respectively), but not consistently with other parameters.
CONCLUSION. In young children, WHtR is not superior to WC or BMI in estimating BF%, nor is WHtR better correlated with cardiometabolic risk factors than WC or BMI in overweight/obese children. These data do not support the use of WHtR in young children.

INTRODUCTION

Various measures are used to detect obesity – defined in terms of excess body fat – and the risk of obesity-related co-morbidities. Body mass index (BMI) is the most commonly used measure, but waist circumference (WC) and waist-to-height ratio (WHtR) as measures of abdominal fat are also used. WHtR may have an advantage over BMI because BMI provides no information about body fat distribution, in particular abdominal fat. Central fat distribution is associated with greater health risks than total body fat (1,2). Therefore, WHtR may be a better indicator of cardiometabolic risk factors than BMI. In adults, WHtR is found to be a better measure than BMI and WC for the prediction of obesity-related cardiometabolic risks factors (3,4). An advantage of WHtR over BMI and WC in adults is that a general cut-off value of 0.5 can be used for both men and women across many ethnicities (3,4). Moreover, the advantage of WHtR over WC is that WHtR adjusts for height. When compared to short people with the same WC, tall people have lower levels of cardiometabolic risk factors and a 30% lower prevalence of the metabolic syndrome (5).

WHtR decreases from birth to the age of five from 0.69 to 0.48 (6), and this decrease continues until early adolescence to 0.40-0.41 (7). From then on it increases slightly to 0.42-0.43 towards the age of 18. Therefore, one cut-off value for all ages during childhood and adolescence is not feasible (6,7). In contrast to adults, it is less clear in young children whether WHtR is better than BMI or WC in predicting obesity-related cardiometabolic risk factors. Most of the studies available evaluated the relationship between WHtR and body fat percentage (BF%) or cardiometabolic risk factors over a large age range, including both children and adolescents, with most studies using children aged 6 years or older. To prevent overweight and obesity in adolescents and adults, early detection of overweight and obesity in young children is needed. During early childhood especially (2 to 6 years of age), excessive BMI gain is predictive of obesity and cardiometabolic risk in adolescence (8) and adulthood (9-11). Furthermore, adipose tissue produces cytokines, like IL-6 and TNFα, which may cause metabolic syndrome, this is already seen in children (12). These cytokines may be a possible link between insulin resistance and adiposity. Increased levels of the separate components of metabolic syndrome have already been demonstrated in children 6 to 9 years old (13). In children aged younger than 6 it is unknown whether these processes are present yet.

Few studies have examined the association between WHtR and BF% (14,15) or cardiometabolic risk factors (15-17) in children aged younger than 6 years. Of the three studies investigating the associations between WHtR and cardiometabolic risk factors in children aged younger than 6 years, only one study analysed the associations between WHtR and more than one cardiometabolic risk factor. Moreover, these studies lack information about overweight/obese children, despite these children being the target group for treatment programmes.

The aim of this study is to assess whether WHtR is a better estimate of BF% than BMI and WC in very young non-obese and obese children (3 to 7 years of age), and whether it is a better indicator of obesity-related cardiometabolic risk factors.

MATERIALS AND METHODS

Subjects

Three groups of children were included in this study. The first group consisted of children (n = 30) from the general healthy Dutch population, 3 and 4 years of age, who were randomly selected from the GECKO Drenthe cohort (18). Data were collected between March 2010 and March 2011. The second group consisted of children (n = 31) from the general healthy Dutch population, 6 and 7 years of age. These children were recruited through advertisements in a local newspaper and on the hospital information site, and by word of mouth. Data were collected in October 2006 and have been partly described in previous studies (19,20). In these two groups, children having medical problems which could affect physical activity, and children diagnosed with a disease or using medication known to affect body composition were excluded from the study. These two groups were combined as one group of children from the general population. The third group consisted of overweight/obese children (n = 75), 3 to 5 years of age, who were part of a randomized controlled clinical trial (GECKO Outpatients Clinic) aimed at reducing overweight (21). The baseline data of the participants were used for this analysis and were measured during the children's first visit to the hospital. Data were collected between October 2006 and March 2008. Only children with overweight or obesity, according to the International Obesity Task Force (IOTF) definitions (22) were included. Children with overweight or obesity due to known medical conditions or eating disorders according to the Dutch Eating Behaviour Questionnaire, mental retardation, severe behavioural problems or other criteria interfering with participation were excluded. Almost all of the children were Caucasian, one child from the first group had an Asian father and two children had African parents (one in the second and one in the third group). Written informed consent was obtained for all children, and the studies were approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG).

Body composition

In all children, height to the nearest 0.1 cm and weight to the nearest 0.1 kg were measured without shoes in light clothing using a stadiometer and a calibrated digital scale, respectively. BMI was calculated as weight/height^2. WC was performed with a standard tape measure and recorded to the nearest 0.1 cm in standing position. WC was measured at the mid-point between the lower costal margin and the level of the anterior superior iliac. BF% was measured using different methods for the three groups. In the first group (3 and 4 years of age from the general population), BF% was determined by the $^2H_2{}^{18}O$ isotope dilution method. Children drank a weighted amount (around 50 grams) of doubly labelled water (Buchem, Apeldoorn, the Netherlands [^2H_2O: 6.02%, $H_2{}^{18}O$: 12.05%]; Campro Scientific, Berlin, Germany [^2H_2O: 6.63%, $H_2{}^{18}O$: 11.50%]). Saliva samples were collected by the parents before administration and approximately 4, 16, 72 and 120 hours after administration. Total body water (TBW) was determined from the dilution spaces of both isotopes. The component TBW in fat free mass (FFM) was set at 0.775 for the 3-year-old boys, 0.770 for the 4-year-old boys, 0.779 for the 3-year-old girls, and 0.777 for the 4-year-old girls (23). BF% was calculated as ([weight-FFM]/weight) * 100. More detailed information is described elsewhere (24). In the second group (6 and 7 years of age from the general population), BF% was calculated from TBW, determined by an orally administered dose of 99.8% ^2H_2O of 0.15 grams per kilogram body weight. Detailed information about the method has been described before (20). In the third group (3 to 5 years of age overweight/obese children), BF% was estimated using a 50 kHz fixed frequency hand-to-foot bio-impedance analyzer (BIA-101, Akern S.r.l./RJL Systems, Florence, Italy). The measurements were performed three times and the average calculated. The resistance (Rz) value from BIA together with height, weight, age and sex were used to calculate the FFM using the Horlick equation (25). BF% was calculated as ([weight-FFM]/weight) * 100.

Overweight/obesity-related cardiometabolic risk factors

Cardiometabolic risk factors were only measured in the overweight/obese group. Systolic and diastolic blood pressures were measured in supine position at the right upper arm with a Dinamap Critikon 1846SX digital sphygmomanometer (Critikon Inc., Tampa, Florida, USA) and an appropriate cuff size. The child was instructed not to speak or move during the measurements. The mean of two measurements was calculated. Blood was drawn after an overnight fast. An enzymatic colorimetric method (Roche Modular, Basel, Switzerland) was used to determine total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol and triglycerides. The updated homeostasis model assessment of insulin resistance (HOMA2-IR) was used to calculate insulin resistance (26). HOMA2-IR was calculated from fasting plasma glucose and fasting plasma insulin, determined by enzymatic method (hexokinase-mediated reaction, Roche Modular, Basel, Switzerland) and radioimmunoassay (Diagnostic Systems Laboratories, Inc., Webster, TX, USA), respectively. Serum levels of leptin, interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNFα) were measured by a combination enzyme-linked immunosorbent assay (ELISA; Milliplex Map Human Adipokine Panel B, Millipore, St. Charles, MN, USA). Serum levels of adiponectin were quantified by ELISA (Millipore, St. Charles, MN, USA).

Statistics

Mean and standard deviations were calculated for all of the characteristics measured. Univariate linear regression analyses were performed with BF% as the dependent variable and WHtR, WC or BMI as the independent factors. In the multivariate linear regression analyses gender and age were added as independent factors. Effect modification of age or gender with WHtR, WC and BMI were checked. Pearson correlations were used to analyse the relationship between the BF% or cardiometabolic risk factors and WHtR, WC or BMI. Statistical analyses were performed using PASW 18.0.3 for Windows (SPSS, Chicago Illinois, USA). The significance level was set to $p < 0.05$ (2-tailed).

RESULTS

Table 1 shows the characteristics of the three groups of children. The children aged 3 and 4 years (n = 30) and 6 and 7 years (n = 31) were representatives of the general population, which was reflected in the number of overweight children, three and six children were overweight, based on the IOTF definitions

(22), respectively. The third group consisted of overweight/obese children aged 3 to 5 years (n = 75). Overweight was present in 38.7% (n = 29) of the children and 61.3% (n = 46) were obese. In addition to the anthropometric measures, the following cardiometabolic measures were also determined in the overweight/obese children: systolic and diastolic blood pressure (113 ± 13 and 64 ± 7 mmHg, respectively), HOMA2-IR (1.0 ± 0.5), leptin (9.4 ± 9.4 ng/mL), adiponectin (18.3 ± 4.7 ng/mL), triglycerides (69.0 ± 33.1 mg/dL), total cholesterol (149.0 ± 23.4 mg/dL), HDL-cholesterol (49.5 ± 10.4 mg/dL), LDL-cholesterol (95.8 ± 20.9 mg/dL), TNFα (3.6 ± 3.2 pg/mL) and IL-6 (1.5 ± 1.2 pg/mL).

Table 1. Anthropometric characteristics in the three groups of children

	3-4 years of age General population (n = 30, 40% boys)		**6-7 years of age General population (n = 31, 56% boys)**		**3-5 years of age Overweight/obese population (n = 75, 28% boys)**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age	3.5	0.3	6.7	0.5	4.7	0.8
Weight (kg)	16.3	1.9	25.1	3.9	28.2	6.5
Height (cm)	101.0	5.4	124.8	6.4	114.9	7.8
Waist (cm)	51.7	2.7	57.0	3.9	64.9	7.5
BMI	15.9	1.2	16.0	1.6	21.1	2.8
WHtR	0.51	0.03	0.46	0.03	0.56	0.05
BF%[a]	22.0[b]	6.4	17.5[b]	5.3	28.3[c]	6.8

BF%, body fat percentage; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio

[a] Data on BF% were missing in four children aged 3 and 4 years, in three children aged 6 and 7 years, and in nine overweight/obese children aged 3 to 5 years

[b] BF% as determined by isotope dilution method

[c] BF% as determined by BIA with Horlick equation

Table 2 shows the associations of BF% with WHtR, WC and BMI. In the crude models, WHtR (r = 0.48, p <0.001) and BMI (r = 0.44, p < 0.001) were associated with BF% in the children from the general population when age groups were combined. In the overweight/obese children, WHtR was correlated with BF% (r = 0.65, p < 0.001), but WC and BMI were even better correlated with BF% (r = 0.81, p < 0.001 and r = 0.81, p < 0.001, respectively). When adjusted for gender and age, WHtR, WC and BMI were significantly associated with BF% in all groups. In the adjusted model for the children from the general population

Table 2. Associations of WHtR, WC and BMI with body fat percentage

	Body fat percentage											
	3-4 years of age			6-7 years of age			3-4 and 6-7 years of age			3-5 years of age		
	General population[1]			General population[1]			General population[1]			Overweight/obese population[2]		
	B [95% CI]	**R^2model**	**Pearson r**	**B [95% CI]**	**R^2model**	**Pearson r**	**B [95% CI]**	**R^2model**	**Pearson r**	**B [95% CI]**	**R^2model**	**Pearson r**
WHtR												
Crude	67.5 [-9.1;144.0]	0.12	0.35	56.2 [-9.5;121.9]	0.11	0.33	72.6 [35.7; 109.6]	0.23***	0.48***	92.9 [66.1;119.8]	0.43***	0.65***
+gender	72.5 [-0.4;145.4]	0.24*		84.1 [20.2;147.9]	0.29*		73.1 [34.7; 111.4]	0.23***		94.5 [66.7;122.4]	0.43***	
+gender,age	94.8 [25.7;164.0]	0.40**		85.8 [20.3;151.3]	0.30*		71.3 [20.5; 122.0]	0.23***		97.4 [71.2;123.7]	0.50***	
WC												
Crude	1.09 [0.24;1.93]	0.23*	0.48*	0.75 [0.30;1.21]	0.31**	0.56**	0.17 [-0.22; 0.56]	0.02	0.12	0.77 [0.63;0.90]	0.66***	0.81***
+gender	1.09 [0.29;1.89]	0.34**		0.89 [0.48;1.30]	0.49***		0.17 [-0.22; 0.57]	0.03		0.80 [0.66;0.94]	0.67***	
+gender,age	0.99 [0.14;1.84]	0.35*		0.93 [0.51;1.36]	0.51***		0.87 [0.42; 1.33]	0.31***		0.87 [0.71;1.02]	0.70***	
BMI												
Crude	1.64 [-0.42;3.70]	0.10	0.32	2.18 [1.24;3.12]	0.46***	0.68***	1.87 [0.79; 2.94]	0.19***	0.44***	2.14 [1.75;2.53]	0.65***	0.81***
+gender	1.72 [-0.25;3.69]	0.22		2.34 [1.50;3.17]	0.61***		1.85 [0.77; 2.93]	0.20***		2.27 [1.87;2.67]	0.67***	
+gender,age	2.14 [0.24;4.03]	0.35*		2.34 [1.49;3.20]	0.61***		1.96 [0.95; 2.97]	0.32***		2.23 [1.82;2.63]	0.68***	

BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio

[1] Body fat percentage measured by isotope dilution method

[2] Body fat percentage measured by BIA with Horlick equation

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

with age groups combined, BMI had the highest explained variance ($R^2 = 0.32$) for BF%. This was also true for the children of 6 and 7 years of age, but WHtR performed best in the children of 3 and 4 years of age. In the adjusted models for the overweight/obese children, WHtR had the lowest explained variance ($R^2 = 0.50$), compared to WC ($R^2 = 0.70$) and BMI ($R^2 = 0.68$). We checked if effect modifications of age or gender with WHtR, WC or BMI were present in the models on top of the adjustments for age and gender. The only significant interaction term was for gender with WHtR in the children from the general population with age groups combined. Adding this term to the model for predicting BF%, the explained variance increased from $R^2 = 0.23$ to $R^2 = 0.33$. This resulted in a beta coefficient of 74.9 for boys and 74.0 for girls. The additional adjustment for interaction with gender makes the explained variance of WHtR, WC or BMI for BF% comparable.

Table 3. Pearson correlation coefficients regarding the associations between cardiometabolic risk factors and WHtR, WC and BMI in overweight/obese children aged 3-5 years (n=75)

	WHtR (r)	**WC (r)**	**BMI (r)**
SBP	0.233*	0.303**	0.361**
DBP	0.076	0.127	0.168
HOMA2-IR	0.534***	0.618***	0.627***
Leptin[a]	0.701***	0.769***	0.779***
Adiponectin	-0.211	-0.311**	-0.152
TG	0.330**	0.364**	0.244*
TC	0.035	0.085	0.056
HDL-C	-0.231*	-0.040	-0.012
LDL-C	0.064	0.033	0.038
TNFα	0.094	0.107	0.158
IL-6	0.030	-0.057	-0.018

BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA2-IR, updated homeostasis model assessment of insulin resistance; IL-6, interleukin-6; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; TNFα, tumour necrosis factor-alpha; WC, waist circumference; WHtR, waist-to-height ratio. Less than 4% of data was missing, with the exception of HOMA2-IR, which was missing in ten children (13%).* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[a] log transformed

Table 3 shows the associations of WHtR, WC and BMI with cardiometabolic risk factors for the overweight/obese children. WHtR, WC and BMI were positively correlated with systolic blood pressure, HOMA2-IR, leptin and triglycerides. For these significant associations, WHtR was not superior to WC and BMI. For adiponectin we found only a significantly inverse correlation with WC and for HDL-cholesterol only an inverse correlation with WHtR.

DISCUSSION

This study revealed that WHtR is associated with BF% in children. However, even after adjustments for gender and age, WHtR is not better associated with BMI and WC. Neither is WHtR a better indicator of most cardiometabolic risk factors than WC and BMI.

WHtR, WC and BMI as indicators of body fat percentage
Previous studies that investigated the association between WHtR and BF% in both normal and overweight children found that WHtR was associated with total or abdominal BF% (15,27-31). Studies in older children (8-16 years of age) showed a better correlation of WHtR with BF% than BMI (27,28). Studies that only included children younger than 10 years have found that WHtR was not better correlated with BF% than BMI or WC (15,29,30). Therefore, this association may be dependent on age. The correlation between WHtR and BF% has been evaluated in only two studies of children of less than 6 years of age (14,15). In these studies the prevalence of overweight/obesity was around 30% (14,15) and the associations were adjusted for age and shown separately for boys and girls. In both studies a significant correlation was found. In our study we also found this significant correlation, both in the overweight obese group as well as in the group from the general population, although the associations seemed to be stronger in the older children (6 and 7 years compared to 3 and 4 years of age). The finding that the association between WC and BF% was initially lost after combining the two age groups in one general population group stresses the importance to look at age-range specific subgroups. But, because WHtR is not better related to BF% than BMI and WC in both the unadjusted and adjusted models, we conclude that WHtR has no advantage over BMI in predicting BF%. It is common to define overweight in children based on the BMI adjusted for gender and age (22). WHtR, either with or without these adjustments, is not a better screening method than adjusted BMI and WC for predicting BF%.

We observed stronger associations between BF% and WHtR, WC and BMI in the overweight/obese group compared to the general population group. An explanation might be that BMI is a better measure of excess body fat in obese children compared to normal weight or overweight children, because BMI is not only dependent on fat mass but also on muscle mass (32), and the higher the fat mass, the smaller the influence of variation in muscle mass. Almost 70% of the children in the overweight/obese group were obese, which may explain why BMI has a higher association with BF% in the overweight/obese group compared to the general population groups. BF% was measured using the isotope dilution method in the general population group, while in the group with overweight/obese children it was assessed by BIA and estimated using the Horlick equation. As expected, BF% was higher in the overweight/obese group compared to the children from the general population group. Even if the BF% may have been underestimated by the BIA method (20) this will not have influenced the correlations with WHtR, WC and BMI, so the difference in methods is not a likely explanation for the higher correlation between the anthropometric measurements and BF%. Moreover, the overweight/obese group consisted of more children than the group from the general population. A group with more children has more power to find a significant effect, but the correlation coefficients will not automatically be higher. Finally, the standard deviations and ranges of WHtR, WC, BMI and BF% were wider in the overweight/obese group, which means a higher chance of finding an association.

WHtR, WC and BMI as indicators of cardiometabolic risk factors

We found only three studies that investigated the relationship between WHtR and one or more cardiometabolic risk factors in children younger than 6 years (15-17). Corvalan et al. assessed the relationship between the anthropometric measures (e.g. WHtR, WC and BMI) and different cardiometabolic markers in 3 to 4-year-old children (15). Whitrow et al. assessed whether WHtR is a better indicator than BMI of SBP in children, 3.5 years of age (17). Campagnolo et al. assessed the accuracy of WHtR, WC and BMI in identifying children (3 and 4 years of age) with multiple risk factors for cardiovascular disease. No correlations between the anthropometric measures and the separate cardiovascular risk factors were found (16).

We found that apart from HDL-cholesterol none of the cardiovascular risk factors were better correlated with WHtR than with BMI or WC (i.e. SBP, HOMA2-IR, leptin and triglycerides). This is in accordance with most previous studies in children aged 4-17 years, based on a review by Browning et al (3). For HDL-cholesterol we found a significant inverse association with WHtR, while no association was found with BMI or WC. This inverse association was also found in a previous review (3), while no association was found in young children (15). The lack of association between total cholesterol and IL-6 with WHtR has also been found in previous studies (3,15). The positive association with triglycerides is consistent with studies in older children, but was not found in young children (15). The absence of an association of WHtR with DBP, adiponectin, LDL-cholesterol and TNFα in young children has not been published before.

A major strength of our study is that the sample was composed of young children of 3 to 7 years of age. In addition, relationships were studied in overweight/obese children. Studies analysing these relationships in young children are limited and we found no studies that analysed these in overweight/obese children at this young age, despite these children being the target population for intervention programmes. The low number of children in the general population groups is a limitation of our study. Although for diagnosis purposes, the cross-sectional design of the study is adequate, the drawback is that it gives no information about the ability of the proxy measures to predict cardio metabolic risk factors later in life. For diagnosis of excess adiposity, cross-sectional data are sufficient, but it would be interesting and very relevant to relate the adiposity measures to future health outcomes.

In conclusion, in young children, either from the general population or overweight/obese, WHtR was not superior to WC or BMI in estimating BF%, nor was WHtR better correlated with cardiometabolic risk factors than WC or BMI in overweight/obese children. These data do not support the use of WHtR in young children.

CONFLICT OF INTEREST

The authors declare there are no competing financial interests in relation to the work described.

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Chapter 4

Energy requirements for maintenance and growth in 3 to 4 year old children are overestimated by existing equations.

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ABSTRACT

BACKGROUND. To give appropriate dietary advice to preschool children, an estimation of their energy requirements is needed. We compared energy requirements for maintenance, measured by indirect calorimetry against existing equations predicting these requirements in 3-4 year old children.
METHODS. In 30 children (age 3.4±0.3) from the GECKO Drenthe cohort, height, weight, evening sleeping metabolic rate (SMR) (by indirect calorimetry), fat mass (FM) and fat free mass (FFM) (by isotope dilution) were measured. Evening SMR, as measure for energy used for maintenance and growth, was compared to existing equations (Schofield, FAO/WHO/UNU, Oxford and Harris-Benedict). Since the equations are based on body size, correlations between SMR, weight, height, FM and FFM were calculated.
RESULTS. All existing equations showed a significant overestimation, ranging from +58 to +144 kcal/day, indicating 8-19% overestimation. This overestimation is higher at lower ranges of energy requirement. SMR was positively related to weight (r=0.488, p=0.013), height (p=0.499, p=0.011) and FFM (r=0.482, p=0.027), but not to FM (r=0.211, p=0.358).
CONCLUSION. Existing equations overestimate energy used for maintenance in young children. Energy used for maintenance is correlated with FFM and not with FM, so energy needs in overweight children may be overestimated more using equations based on weight only.

INTRODUCTION

The overweight epidemic is growing worldwide. Alarming is the rapid increase in overweight in young children and adolescents. The global prevalence of overweight and obesity is estimated to be 6.7% in children of 0 to 5 years of age. In developed countries, overweight and obesity are currently more common in this young age-group, up to 11.7% in developed countries (1). The cause of this epidemic is multi factorial, including dietary factors, activity patterns and genetic background (2). The evidence for higher effectiveness for early intervention to prevent obesity is growing. Intervention in 3 to 5 year old children can successfully decrease BMI Z-scores and adiposity (3). A Swedish obesity center reported that initiation of treatment at younger age results in larger treatment effect (4). In order to give appropriate dietary advice to parents of young children, it is necessary to have an estimation of the needs of the child, including the energy needs. Total energy expenditure (TEE) includes energy needed for maintenance, activity and growth. TEE in children has been measured by the doubly labeled water (DLW) technique and from studies using heart rate monitoring (HRM) (5). Energy requirements for maintenance are considered equal to the basal metabolic rate (BMR). The energy requirements for maintenance can be measured by calorimetry, but are usually estimated from existing equations. The equations most used are from Schofield (5), the FAO/WHO/UNU (6), the Oxford equations (7) and those published by Harris-Benedict (8).

The FAO/WHO/UNU published in 1985 estimations of the total energy requirements based on the Schofield equations using weight only, added with an activity factor of 1.4 (6). The FAO/WHO/UNU concluded in 2001, based on measurements using DLW and HRM that the TEE in children of less than eight to ten years is lower than estimated in 1985 (5). For the estimation of the energy for maintenance, the same Schofield formula was used. The energy used for activity was calculated as the difference between the doubly water results and the results of the Schofield method (5). Whether the lower measured energy needs of children is caused by a lower BMR than estimated, or by a lower level of activity than the estimated activity factor, is not clear from this report. In the last FAO/WHO/UNU recommendation a multiplication factor of 1.4-1.5 for activity energy expenditure was given (5). The equation to calculate the energy requirements for maintenance used in both reports of the FAO/WHO/UNU was a slightly adapted equation from Schofield (1985), some additional data were included by the authors of that analysis (6). Another equation of Schofield, not used by the WHO/FAO/UNU, added height to the BMR equation. When taking a closer look at the studies used to calculate the Schofield equations, we can identify some limitations. The studies were performed in the thirties and sixties of the last century with systems that may not be as reliable as modern calorimeters (7). Furthermore, the number of young children included in the studies from which the equations are made is rather small, and the circumstances under which the measurements were done, like fasting or not, thermo neutral or not, are not very clear. When the estimated energy needs of young children are too high, incorrect advice might be given to children, causing the risk to develop childhood overweight.

The aim of this study was to measure energy requirements for maintenance in 3 and 4 year old children by indirect calorimetry under standardized conditions and to compare these results with existing equations. Since the equations are based on body mass, we additionally related these energy requirements to body weight, height, fat mass (FM) and fat free mass (FFM) of the child.

METHODS

This study is part of a study on activity patterns, total energy and resting energy expenditure in 3 and 4 year old children. Part of the results of the indirect calorimetry measurements have been published before to calculate the energy used for activity (8).

Participants

Thirty healthy preschool children (age 3.4 ± 0.3, range 3.1 – 4.1 years) from the Netherlands were randomly selected from the population-based GECKO Drenthe birth cohort (www.birthcohorts.net) (9). Written informed consent was obtained from both parents and the study was approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG).

Measurements

Height to the nearest 0.1 cm and weight to the nearest 0.1 kg were measured, without shoes in light clothing using a calibrated digital scale and a stadiometer, respectively, according to a standardized protocol by the researcher in the afternoon on the test day at the child's home.

Energy used for maintenance
The energy used for maintenance, including growth, was estimated by measuring evening sleeping metabolic rate (SMR) by indirect calorimetry (Deltatrac II MBM-200 metabolic monitor, Datex Ohmeda, Finland) (10) in the evening of the test day at the child's home. Measurements were done when the child was asleep in his/her own bed. After stable values were reached, the measurement was done over 30 minutes. A hood was placed over the head of the child and concentrations of oxygen and carbon dioxide were measured together with the flow rate of the air entering and leaving the hood. The metabolic rate was calculated by the calorimeter from the oxygen consumption and the carbon dioxide production. In the calculation the contribution of the protein oxidation was not taken into account, as it has been shown that protein oxidation has a very small effect of the calculation of the energy expenditure from results of the indirect calorimetry (11). If the child woke up, the hood was removed and the measurement was started again when the child was back asleep. If this failed, we tried it on another evening within two weeks.

The energy for maintenance is considered to be equal to the BMR. Measuring BMR (defined as energy expenditure in resting state, supine, under thermoneutral conditions, during fasting) in infants and young children is not feasible, since the child must be fasted for 12 hours and – more problematic- is asked to stay awake but quiet during at least 30 minutes while situated under a ventilated hood system. Therefore, evening SMR is used as a measurement as close to the BMR as possible. The rationale for this is that energy used for diet induced thermogenesis, as it is already shown by Brooke and Asworth in 1972, is in fast growing children related to the rate of growth (12). The energy requirements for growth therefore includes the diet induced thermogenesis. This also indicates that growth takes place especially after a meal (11-14). The energy for diet induced thermogenesis in adults, is normally not included in the BMR. However, in children it is appropriate to take it into account as energy for basal energy requirements. We measured the sleeping metabolic rate in our cohort 1-2 hours after a meal. This way, the energy used for growth, or for diet induced thermogenesis is included in the sleeping metabolic rate as measured by us.

For the comparison with the data obtained in this study, the four equations, shown in Table 1 were used.

Table 1. Published equations to calculate basal metabolic rate (kcal/day)

1. Schofield equation (weight and height) for age 3-10 years (7):	
Boys	19.6*weight (kg) + 130*height (m) + 415
Girls	17.0*weight (kg) + 162*height (m) + 371
2. FAO/WHO/UNU equation for age 3-10 years (6):	
Boys	22.7*weight (kg) + 495
Girls	22.5*weight (kg) + 499
3. Oxford equation (weight and height) for age 3-10 years (15):	
Boys	15.1*weight (kg) + 314*height (m) + 306
Girls	15.9*weight (kg) + 210*height (m) + 349
4. Harris-Benedict equation for all ages (16):	
Boys	5.003*height (m) + 13.752*weight (kg) - 6.755*age (yrs) + 66.473
Girls	1.850*height (m) + 9.563*weight (kg) - 4.676*age (yrs) + 655.096

Body composition

A stable isotope dilution method was used to measure the body composition. After a baseline saliva sample at day 0, participants drank a weighted amount (around 50,000 grams) of DLW (Buchem, Apeldoorn, The Netherlands [^2H_2O: 6.02%, $H_2{}^{18}O$: 12.05%]; Campro Scientific, Berlin, Germany [^2H_2O: 6.63%, $H_2{}^{18}O$: 11.50%]). Saliva samples were collected by the parents before administration and approximately 4, 16, 72 and 120 hours after administration. Total body water (TBW) was calculated using the dilution spaces of both isotopes. The component TBW in FFM was set at 0.775 for the 3-year-old boys, 0.770 for the 4-year-old boys, 0.779 for the 3-year-old girls, and 0.777 for the 4-year-old girls (17). From FFM and weight, FM, %FM and %FFM were calculated. The method is described in detail before (18).

Statistics

Pearson correlations and Bland-Altman plots were used to compare measured evening SMR with estimated BMR calculated from equations. Mean difference between the two methods was calculated and tested against zero using a one-sample t-test. Pearson correlations were also used to calculate the correlation between SMR and weight, height, FM and FFM. Prediction models of SMR were calculated using linear regression analyses with weight or weight and height as prediction factors. Data are presented as mean ± SD, and range (min-max). Statistical analyses were performed using SPSS 20.0.0.1 for Windows (SPSS, Chicago Illinois, USA). For Bland-Altman analysis GraphPad Prism 5.04 for Windows (GraphPad Software, San Diego California USA, www.graphpad.com) was used. The significance level was set at $P < 0.05$ (2-tailed).

RESULTS

In 25 of the 30 children reliable data of the SMR could be obtained. The other children woke up repeatedly, making reliable measurements impossible. Clinical characteristics of these 25 children are shown in Table 2. One child was overweight and 1 child obese. Lean body mass ranged from 9.8 to 15.2 kg, %FM from 11.8 to 35.2%.

Table 2. Characteristics of the subjects

	n	Mean ± SD	Range (min-max)
Age, yrs	25	3.4 ± 0.3	3.1- 4.0
Weight, kg	25	16.1 ± 1.8	12.1- 19.8
Height, m	25	100.4 ± 5.6	86.0- 113.1
BMI, kg/m^2	25	15.9 ± 1.2	14.1- 19.3
FM, kg	21	3.8 ± 1.2	1.8- 6.9
%FM	21	23.1 ± 6.5	11.8- 35.2
FFM, kg	21	12.4 ± 1.3	9.8- 15.2
%FFM	21	76.9 ± 6.5	64.8- 88.2
SMR, kcal/day	25	765 ± 88	610- 920
SMR, kcal/kg/day	25	47.9 ± 5.5	35.3- 58.9
BMRest Schofield (7), kcal/day	25	824 ± 44	763- 937
BMRest FAO/WHO/UNU (6), kcal/day	25	860 ± 41	770- 945
BMRest Oxford (15), kcal/day	25	830 ± 44	758- 949
BMRest Harris-Benedict (16), kcal/day	25	908 ± 116	643- 1016

FFM: fat free mass; FM: fat mass, BMRest: estimated basal metabolic rate, SMR: sleeping metabolic rate

The average SMR was 765 ± 88 kcal/day or 48 ± 6 kcal/kg/day. There was no difference between the SMR in boys (49 ± 7 kcal/kg/day, n = 8) compared to girls (47 ± 5 kcal/kg/day, n = 17). The SMR calculated from the four equations was higher for all equations, Schofield 824 ± 44 kcal/day (+8%), FAO/WHO/UNU 860 ± 41 kcal/day (+12%), Oxford 830 ± 44 kcal/day (+8%) and Harris-Benedict 908 ± 116 kcal/day (+19%). Correlations between SMR and calculated BMR were moderate for Schofield with Pearson $r = 0.45$ ($p = 0.02$, $R^2 = 0.21$), for FAO/WHO/UNU, $r = 0.49$ ($p = 0.01$, $R^2 = 0.24$) and for Oxford, $r = 0.49$ ($p = 0.01$, $R^2 = 0.24$) but was not significant for Harris-Benedict, $r = 0.18$ ($p = 0.39$,

$R^2 = 0.03$). The Bland-Altman plots of the comparison between the different results are given in figure 1. All equations showed a significant overestimation of BMR, ranging from +58 to +143 kcal/day, which is an 8-19% overestimation. However, it is important to note that this overestimation depends on the level of BMR, and is higher at lower ranges of BMR. In the Harris-Benedict equation, the differences between estimates for boys and girls are high. The estimates are comparable to our measurements in boys, but deviate considerably in girls.

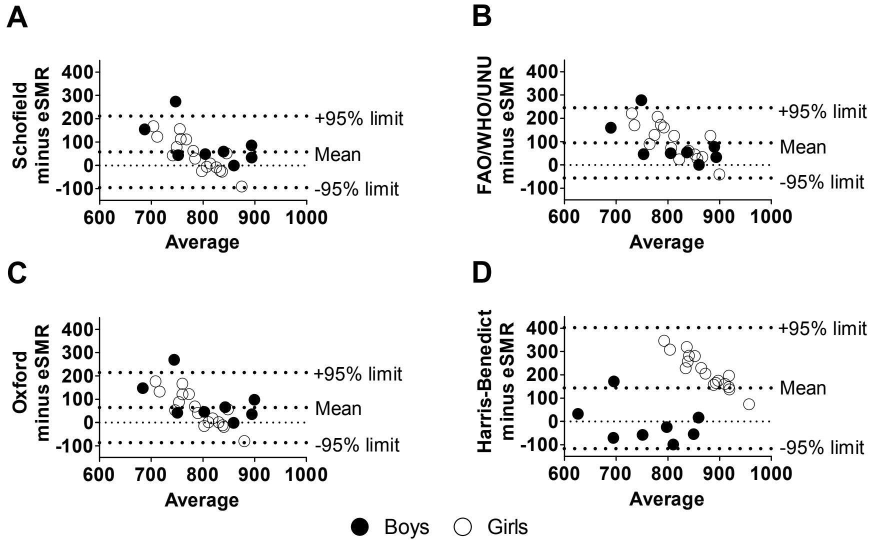

Figure 1. Measured evening sleeping metabolic rate (eSMR) vs. estimated basal metabolic rate (BMR) according to Schofield (A), Oxford (B), FAO/WHO/UNU (C), and Harris-Benedict (D) equations. Average: the average value of eSMR and the BMR according to the equation. A: Mean difference (bias): 58 ± 78 kcal/day (8% of mean eSMR) and 95% limits of agreement of -95; 212 (-12; 28% of mean SMR), p = 0.001. B: Mean difference (bias): 95 ± 77 kcal/day (12% of mean eSMR) and 95% limits of agreement of -56; 246 (-7; 32% of mean SMR), p < 0.001. C: Mean difference (bias): 65 ± 77 kcal/day (8% of mean eSMR) and 95% limits of agreement of -86; 215 (-11; 28% of mean SMR), p < 0.001. D: Mean difference (bias): 144 ± 132 kcal/day (19% of mean eSMR) and 95% limits of agreement of -116; 403 (-15; 53% of mean SMR), p < 0.001.

The SMR was positively related to body weight (r = 0.488, p = 0.013), height (p = 0.499, p = 0.011) and FFM (r = 0.482, p = 0.027), but not to FM (r = 0.211, p = 0.358). Based on the regression analysis between SMR and weight, the following equation for the energy requirements for maintenance (kcal/day) would fit our data in 3 and 4 year old children best: 24*weight (kg) + 380 (R^2 =

0.24, p = 0.01). Adding height slightly improved the R^2 (from 24 to 28% explained variance) but predictors were no longer significant.

DISCUSSION

In this study we found lower values for energy requirements for maintenance and growth estimated by evening SMR, than when calculated from existing equations for the BMR in children. The difference between energy used for maintenance from measured SMR and BMR equations depended on the level of BMR, and overestimation was higher at lower ranges of BMR, indicating that energy expenditure was overestimated especially in children of younger age or lower weight.

There might be different explanations for our findings. First, we measured SMR and not BMR. BMR is defined as the metabolic rate measured while being quiet in the awake state, after an overnight fast in the thermoneutral environment (5). It is, for ethical and practical reasons, impossible to measure the BMR in 3-year old children, as it is highly unlikely that they will stay quiet for more than 10 minutes under a ventilated hood when awake, while fasting. The energy requirements for growth includes the diet induced thermogenesis and growth takes place especially after a meal. We measured the sleeping metabolic rate in our cohort 1-2 hours after a meal. This way, the energy used for growth, or for diet induced thermogenesis is included in the sleeping metabolic rate as measured by us. The contribution of the dietary induced thermogenisis or energy used for growth is rather small in young children. Studies have shown that the energy required for tissue synthesis is around 2 kcal/gram growth. The growth of a 3 or 4 year old child is around 6 gram/day (5). The energy used for growth by these children therefore only is 12 kcal/day, which implies a minimal effect on the energy balance. So, we included in our measured energy for maintenance, the energy used for growth as well as the energy expended in diet induced thermogenesis, where the energy used by these processes is rather low in young children.

Secondly, we could not trace if the pre-specified conditions for BMR were followed during the studies that were published fifty and more years ago. One recent study measured overnight sleeping metabolic rate and BMR in 10 year old children. This study found a lower average overnight SMR (OMR) than morning BMR. OMR was calculated from all results obtained during the whole night. OMR was not constant during the night, minimal values were found in the middle of the night compared to the beginning (19). They conclude that in young adults, the ratio for OMR/BMR was 1.0, but in 10-year old children OMR/BMR was 0.92, suggesting that BMR measured under standardized conditions overestimates daily energy requirements in children (19). We measured SMR shortly after the children fell asleep, so in the beginning of the night. Moreover, the children had a meal 1-2 hours before, a period when the metabolic rate is higher compared to the fasted state due to the so called diet induced thermogenesis, in children considered the energy used for growth (12). If a deviation from BMR is expected, the evening SMR would thus rather be higher than the (morning) BMR, instead of lower.

Taking this together, we do not believe that the lower SMR data as found by us can be explained from the difference in conditions between SMR and BMR. In addition to the suggestion that (morning) BMR may overestimate basal energy requirements in children, the most likely explanation is that the results are due to differences in the apparatus used in the past to measure the BMR. The Schofield equation is based on rather old data, some of them are from the thirties of the past century. The Harris-Benedict equation is based on measurement of only the CO_2 production. The higher values for BMR found in the past are most likely caused by less accurate calorimeters. Some older studies used closed indirect calorimeters, where it is found that these systems tend to overestimate the oxygen consumption as they are very sensitive to leaks and cannot measure CO_2 production (15,20). The calorimeter, as used by us, measured both consumed O_2 and produced CO_2, was calibrated before each measurement against test gas and has shown to have a high accuracy and reproducibility (10).

We found that the overestimation of energy used for maintenance was related to the weight of the children, a higher overestimation was found in the youngest children with a lower weight. In the older and larger children, most close to the mean age for which the equations were developed, less discrepancy was found between measured and estimated energy used for maintenance. In the Schofield, FAO/WHO/UNU and Oxford equation one equation is given for the age range of 0-3 years and one for age range 3-10 years. This also might be an explanation for our findings, as it is a well-known phenomenon that the error increases at the boundaries of the population for which the prediction equation was developed. Moreover, only few measurements in children of 3 years were included by Schofield, contributing further to a chance of error in the estimates. Since the equations in this young age group may lead to errors, it may be less suitable for use in 3- and 4-year-old children. The equation for the calculation of the BMR as formulated by the Oxford group, published after the latest FAO/WHO/UNU report, results in slightly higher values for boys of 3-10 years, but lower values for girls compared to the FAO/WHO/UNU equation. The difference between both equations is the inclusion of a high percentage Italians in the FAO/WHO/UNU report and more participants from developing countries in the Oxford equation.

Our findings of a lower amount of energy used for maintenance than estimated from previously published equations is in line with the latest FAO/WHO/UNU report showing that the TEE is lower in children up to 8-10 years than previously estimated. A lower TEE, as found in the latest FAO/WHO/UNU report, might either be due to a lower level of activity or a lower amount of energy used for maintenance. In our previous paper, higher values of physical activity level were found than given in the FAO/WHO/UNU report, 1.6 vs. 1.44 (5,8). It is unlikely therefore that the lower values of TEE are due to a lower level of activity. More likely the older equations lead to an overestimation of the BMR.

We found for the first time in young children that SMR is positively correlated with the FFM, while there was no relation with the FM. The same results were found by Heymsfield et al. in adults (21). FFM is much more metabolically active than FM. For young children this implies that stimulation of activity will help to reduce the risk of overweight by increasing the FFM. It also indicates that calculating the energy needs on the basis of only the weight might result in an overestimation of the needs in overweight/obese children, as overweight is related to a higher amount of, energetically less active FM.

In our study we could not confirm that there is a difference in SMR between boys and girls, but this might be due to the rather low number of boys included in our study. In that respect, it is a drawback of the study that because of the costs of the doubly labeled water, only 30 children were included. Based on our results, we suggest that the formula: energy used for maintenance (kcal/day) = 24* weight (kg) + 380 can be used for validation studies to improve the estimates of energy needs in 3 and 4 year old non overweight children.

In conclusion, existing BMR equations overestimate the energy used for maintenance in children aged 3 and 4 years old. Furthermore, energy used for maintenance is correlated with FFM and not with FM, indicating that energy needs in overweight children would be more overestimated than in normal weight children using equations based on weight only.

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Chapter 5

Validation of the TracmorD tri axial accelerometer to assess physical activity in preschool children

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Obesity 2013, in press

ABSTRACT

OBJECTIVES. The aim of this study is to assess validity evidence of Tracmor$_D$ to determine energy used for physical activity in 3 to 4-year old children.
DESIGN AND METHODS. Participants were randomly selected from GECKO Drenthe cohort (n=30, age 3.4±0.3 years). Total energy expenditure (TEE) was measured using the doubly labeled water method. Sleeping metabolic rate (SMR) was measured by indirect calorimetry (Deltatrac). TEE and SMR were used to calculate physical activity level (PAL) and activity energy expenditure (AEE). Physical activity was monitored using a DirectLife tri axial accelerometer, Tracmor$_D$ with activity counts/minute (ACM) and activity counts/day (ACD) as outcome measures.
RESULTS. The best predictors for PAL and AEE were ACM with gender and weight; and ACM alone, respectively (backward regression, R^2=0.50, p=0.010 and R^2=0.31, p=0.011, respectively). With ACD, the prediction model for PAL included ACD, height, gender and sleep duration (R^2=0.48, p=0.033), the prediction model for AEE included gender and sleep duration (R^2=0.39, p=0.042). In our study the accelerometer was worn for 5 days, but 3 days did not give a different estimated PAL.
CONCLUSION. Tracmor$_D$ provides moderate-to-strong validity evidence that supports its use to evaluate energy used for physical activity in 3 to 4-year old children.

INTRODUCTION

Overweight and obesity are a considerable health problem in developed countries. Not only in adults but also in children the prevalence of obesity is growing (1,2). Children with overweight or obesity have a higher chance to be obese in adulthood than children without this condition (3). To prevent obesity and related co morbidities, risk factors early in life need to be investigated. Low physical activity and high sedentary behavior are known risk factors for overweight and obesity in adults (4) and children (5). Also in preschool children it is suggested that physical activity is inversely related to percentage body fat, but more studies are needed to draw firm conclusions (6). Besides the predictive value of physical activity on the development of obesity, obesity discourages physical activity, which promotes further weight gain (7). Validated devices to evaluate physical activity in preschoolers are necessary for valid results. Physical activity can be defined as any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level. The energy used for physical activity, the activity energy expenditure (AEE), can be calculated from the total energy expenditure (TEE) minus the basal metabolic rate (BMR) (or sleeping metabolic rate (SMR)) and diet induced thermogenisis (about 10% of total energy intake). BMR and SMR can be measured by indirect calorimetry. Another method is to calculate the physical activity level (PAL) as TEE/BMR (or SMR) (8). Measuring TEE by the doubly labeled water (DLW) method is generally accepted as 'the gold standard'. Disadvantages of the DLW method are that it is expensive and both the DLW method and the indirect calorimetry are time consuming. A relative new device for measuring physical activity is the tri axial accelerometer. A tri axial accelerometer has shown to measure reliably physical activity during the day in adults (9,10) and children (11). Next to the total AEE and PAL, it provides information about duration, frequency and intensity of the physical activity. Few studies have investigated the validity of tri axial accelerometers in young children aged 4-6 years (12,13). So far the Tracmor$_D$ was only validated in adults, the outcome of the Tracmor$_D$ explained 46% of the variance in AEE and PAL (10). From the perspective of prevention of obesity, it is important to validate the tri axial accelerometers in children aged younger than 5 years. Therefore, the aim of this study is to assess validity evidence of the Tracmor$_D$, a tri axial accelerometer, to determine energy used for free-living physical activity in 3 to 4-year old children.

METHODS AND PROCEDURES

Participants

Thirty preschool children aged 3 to 4 years old, living in Drenthe, one of the northern provinces of The Netherlands participated in this study. They were randomly selected from the GECKO-Drenthe birth cohort (n = 2997 signed informed consent and n = 2629 are still participating). GECKO-Drenthe is a population-based birth-cohort studying the risk factors for overweight in young children (14). The inclusion criterion for this validation study was born in January, February or March 2007. The exclusion criterion was having medical limitations which could affect physical activity. Written informed consent was obtained, and the study was approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG).

Body composition

Anthropometric measurements were carried out in the afternoon on day 0 at the child's home. Height to the nearest 0.1 cm and weight to the nearest 0.1 kg were measured without shoes in light clothing using a calibrated digital scale and a stadiometer, respectively. Body mass index (BMI) was calculated as weight(kg)/height^2(m).

Sleeping metabolic rate

SMR was measured using a ventilated hood: the Deltatrac II MBM-200 metabolic monitor (Datex Ohmeda, Finland). The Deltatrac is an open system indirect calorimetry device that measures $\dot{V}O_2$ and $\dot{V}CO_2$ and, from these variables, calculates the respiratory quotient (RQ = $\dot{V}CO_2$ / $\dot{V}O_2$) and energy expenditure (15). In the evening of day 0 at the child's home, during sleep, the child was covered with a ventilated hood for 30 minutes. The measurement of $\dot{V}O_2$ and $\dot{V}CO_2$ started after the gasses were stable in the hood (approximately after 5 minutes). When the child woke up, the hood was removed and the measurement was started again after the child falling back asleep. When the child woke up and wouldn't sleep anymore we tried to obtain the measurement on another evening within two weeks.

Total energy expenditure

TEE was measured with the DLW method. After a baseline saliva sample at day 0, participants drank a weighted amount (around 50,000 grams) of DLW (Buchem, Apeldoorn, The Netherlands (^2H_2O: 6.02%, $H_2{}^{18}O$: 12.05%); Campro Scientific, Berlin, Germany (^2H_2O: 6.63%, $H_2{}^{18}O$: 11.50%)). Participants drank the

DLW from a tube with a straw. Before and after drinking, the tube with the straw was weighted on a calibrated digital scale in milligrams. Saliva samples were collected by the parents at approximately 4, 16, 72 and 120 hours after administration of the DLW dose, who recorded the exact date and time of the collection. Saliva was sampled by swabbing a pre-dried cotton rod (Sugi® Kettenbach, Eschenburg, Germany) in the child's mouth for 1-2 min and then putting the cotton rod in an airtight plastic container. Participants were not allowed to eat or drink for 30 min prior to saliva sampling. Parents stored the saliva sample in their refrigerator (0-7°C) till the researcher visited the child at day 6 or 7 to pick up the saliva samples and the accelerometer. From then the saliva samples were stored frozen at -80°C prior to analysis. Enrichment of the ^{2}H and ^{18}O isotopes in the samples was measured in quintuplet by a high-temperature conversion elemental analyzer coupled with a Delta XP isotope-ratio mass spectrometer via a Conflo-III Interface (Thermo Fisher, Bremen, Germany) as described previously (16). The results of every first two analyses were skipped and the main of the results of every last three analyses was used for calculation of the total body water (TBW). TBW was calculated by estimating the isotope dilution spaces (IDS) of ^{2}H and ^{18}O. Dilution space is calculated by determining the intercept of ^{2}H and ^{18}O, using the isotope dilution at 3 time points.

$$TBW = \frac{\frac{IDS_{2H}}{1.041} + \frac{IDS_{18O}}{1.007}}{2}$$

The constants 1.007 and 1.041 were included to adjust for the differences between the IDS and TBW due to isotope exchange (17). TBW was used to calculate rCO_2 using the following equation, which is an adapted version by Racette (17) of the original data by Schoeller (18).

$$rCO_2 = (TBW / 2.078)(1.007K_O - 1.041K_D) - 0.0246R_{Gf}$$

where K_O and K_D are the ^{18}O and ^{2}H isotope disappearance rates, respectively; and rGf is the rate of water loss trough gaseous routes subject to isotope fractionation. The latter is estimated as $1.05TBW(1.007K_O - 1.041K_D)$ (19).

TEE was calculated by using the modified Weir's equation (20) from the measured mean daily carbon dioxide production rate (in mol/d):

$$TEE(kcal / day) = \frac{3.9rCO_2}{RQ} + 1.1rCO_2$$

The rCO_2 is expressed in L/day and can be converted from mol/day by multiplying by 22.4. The respiratory quotient (RQ) is oxygen consumption /rCO_2 (19). It was assumed that children did not lose or gain weight during the measurement period. Without over or under eating the food quotient most closely approximates the RQ during the day (21). Food quotients were estimated according to the RIVM macro nutrient intake for age and gender in the Netherlands (22). The values of the food quotients were 0.884 for the 3 year old boys, 0.881 for the 4 year old boys, 0.885 for the 3 year old girls and 0.882 for the 4 year old girls. More detailed information about the calculations of TBW, rCO_2 and TEE is described previously (19). AEE was calculated as TEE – SMR. The physical activity level (PAL) was calculated as TEE/SMR (8).

Accelerometry

The DirectLife tri axial accelerometer for movement registration, Tracmor$_D$ (Philips DirectLife, Amsterdam, The Netherlands) was used to estimate the free-living physical activity for 5 consecutive days during waking hours except for water activities. The accelerometer was worn at the same days as when the TEE was measured by the DLW method. Parents reported sleeping and wake times and times of wearing the accelerometer. The Tracmor$_D$ is a tri axial accelerometer, equipped with a piezo-capacitive accelerometer, which allows the detection of both dynamic and static accelerations. It measures 3.2 x 3.2 x 0.5 cm and weights 12.5 grams (battery included). Because of its small size and light weight the Tracmor$_D$ does not interfere with daily activities. The accelerometer was worn in the middle of the lower back in a small case on a belt. Detailed information about the Tracmor$_D$ has been described before (10). Accelerometer output (counts/minute) is based upon a 20Hz measurement of the x-axis, y-axis and z-axis. Output of the accelerometer, as mean of all 3 axis of measurement, is defined as mean activity counts per minute (ACM) and as mean total activity counts per day (ACD). ACM is calculated as the sum of all counts/min during the wear period divided by the total amount of wear time in minutes. ACD is calculated as the sum of all counts/min of wear time of the valid days divided by the amount of valid days. A day was invalid when the time during which they wore the accelerometers and the time spent sleeping did not add up to at least 19 hours.

Statistics

Pearson correlations and linear regression analyses were made with TEE, AEE or PAL as dependent variable and ACD or ACM as independent variables. Prediction models of AEE and PAL were calculated using linear backward regression analyses with weight, gender, sleep duration and ACM or ACD as prediction factors (entry criteria: 0.20, removal criteria: 0.25). Prediction models of TEE were calculated using linear backward regression analyses with SMR, weight, gender, sleep duration and ACM or ACD as prediction factors (entry criteria: 0.20, removal criteria: 0.25). All regression models were checked on multicollinearity (<0.7), and the residuals had to be normally distributed. To see if 3 instead of 5 days are enough to make a valid estimation of the PAL, a Bland-Altman plot was made with estimated PAL calculated with 5 days of physical activity measurement as reference variable and estimated PAL with the first 3 days of physical activity measurement as the alternative variable. Mean difference (bias) between the two methods was calculated and tested against zero using a one-sample t-test. Statistical analyses were performed using SPSS 16.0 for Windows (SPSS, Chicago Illinois, USA). Difference between the children who were excluded and included for analyses and difference between boys and girls were tested with a Chi square for variables at interval/ratio level, an independent t-test for the normal distributed variables at nominal level and a Mann-Whitney test for the non parametric variables at nominal level. Graphs were made using GraphPad Prism 5.04 for Windows, (GraphPad Software, San Diego California USA, www.graphpad.com). The significance level was set to $p < 0.05$ (2-tailed).

RESULTS

Thirty children were included in this study. In Table 1 the participant characteristics are shown. Mean accelerometer wear time was 10.0±1.2 hours/day; mean SMR was 765±88 kcal/24 hours and mean TEE was 1301±193 kcal/24 hours (table 1). Two children were overweight and 1 child was obese according to the BMI cut-off points of Cole et al. (23). No significant differences were found between boys and girls. In 5 children (4 boys, 1 girl) it was not possible to measure the SMR, because they woke up every time we tried. Four children (3 boys, 1 girl) had no valid TEE data. One girl had no accelerometer data because of battery problems. Twenty-five children had complete data to perform the analyses for the prediction model of TEE. Twenty children had complete data to perform the analyses for the prediction model of PAL and AEE. Of those 20 children mean TEE = 1260±166, AEE = 484±169, SMR = 776±85 and PAL = 1.6±0.3. The children not included in the analyses consisted of significantly more boys than girls ($\chi^2 = 5.6$, $p = 0.02$), for the other characteristics from Table 1 no significant differences were found between the included and not included children. For the prediction of TEE from the ACD, the measurement was based on 3 valid wear days in 1 child, on 4 valid days in 4 children, and on 5 valid days in 20 children. For the prediction of AEE and PAL from the ACD, the measurement was based on 3 valid wear days in 1 child, on 4 valid days in 2 children, and on 5 valid days in 17 children.

Table 1. Participant characteristics

	N	Mean ± SD	Range (min-max)
Boys/girls (n)	30	12/18	
Age (years)	30	3.5 ± 0.3	3.1 - 4.1
Height (m)	30	101.0 ± 5.4	86.0 – 113.1
Weight (kg)	30	16.3 ± 1.9	12.1 – 21.2
BMI (kg/m^2)	30	15.9 ± 1.2	14.1 – 19.3
Sleep duration (hours/day)	30	12.4 ± 0.9	10.0 – 14.6
Wear time (hours/day)	29	10.0 ± 1.2	7.3 – 11.6
Sleep and wear time (hours/day)[1]	29	22.4 ± 1.0	20.0 – 23.9
Daily PA (ACM)	29	3666 ± 579	2791 – 4980
Daily PA (ACD)*10^5	29	23 ± 4.7	16 – 35
Valid wear days	29	4.8 ± 0.5	3 - 5
SMR (kcal/day)	25	765 ± 88	610 – 920
TEE (kcal/day)	26	1301 ± 193	1017 – 1734
AEE (kcal/day)	21	485 ± 165	186 – 781
PAL (TEE*SMR^{-1})	21	1.6 ± 0.2	1.2 – 2.1

ACD: activity counts per day, ACM: activity counts per minute, AEE: activity energy expenditure, kg: kilogram, m: meter, PA: physical activity, PAL: physical activity level, SD: standard deviation, SMR: sleeping metabolic rate, TEE: total energy expenditure.

[1] For valid days only

Mean ACM and mean ACD were significantly correlated with PAL (r = 0.61; p = 0.004 and r = 0.46; p = 0.042, respectively). Mean ACM was significantly correlated with AEE (r = 0.56, p = 0.011), but no correlation between mean ACD and AEE was found (r = 0.38, p = 0.098). Mean ACM and mean ACD were not correlated with TEE (r = 0.34; p = 0.094 and r = 0.21; p = 0.326, respectively). The univariate regression analysis of PAL and AEE with ACM or ACD as prediction factors are shown in Table 2.

Next to the univariate regression analysis, the multivariate backward regression outcome is shown in Table 2. ACM, gender and weight explained 50% of the variance in PAL (p = 0.010), ACM without other variables included explained 31% of the variance in AEE (p = 0.011). The ACD, height, gender and

Table 2. Prediction models of PAL, AEE and TEE.

	ACM as PA outcome				ACD as PA outcome		
	B	**95% CI**	**R^2**		**B**	**95% CI**	**R^2**
PAL[1]							
Univariate model							
Intercept	0.55			Intercept	0.97		
ACM*10^{-4}	2.96	1.06-4.87		ACD*10^{-7}	2.93	0.12– 5.75	
			0.37**				0.21*
Multivariate model[a]							
Intercept	1.04			Intercept	0.265		
ACM*10^{-4}	2.86	1.04- 4.69		ACD*10^{-7}	4.24	1.16- 7.33	
Weight	-0.044	-0.102- 0.014		Height	-0.011	-0.030- 0.008	
gender	0.15	-0.06- 0.36		Sleep	0.096	-0.022-0.213	
			0.50**	Gender	0.195	-0.033-0.424	
							0.48*
AEE[1]							
Univariate model							
Intercept	-189.8			Intercept	110.6		
ACM	0.183	0.048 – 0.319		ACD*10^{-4}	1.65	0.34- 3.64	
			0.31*				0.15
Multivariate model[a]							
Intercept	-189.8			Intercept	-1412		
ACM	0.183	0.048 – 0.319		ACD*10^{-4}	2.93	0.82- 5.04	
			0.31*	Gender	122.3	-38.0- 282.5	
				Sleep	82.8	1.9- 163.8	
							0.39*
TEE[2]							
Multivariate model[a]							
Intercept	-19.9			Intercept	-1170		
ACM	0.173	0.022-0.323		ACD*10^{-4}	2.71	0.37- 5.05	
SMR	0.831	-0.0.85-1.746		Sleep	82.48	-0.83- 165.80	
			0.29	SMR	0.77	-0.17-1.70	
				Gender	117.57	-48.41-283.54	
							0.38

P value model * $p < 0.05$, ** $p < 0.01$; ACD: activity counts per day, ACM: activity counts per minute, AEE: activity energy expenditure, CI: confidence interval, PA: physical activity, PAL: Physical activity level, SMR: sleeping metabolic rate, TEE: total energy expenditure; [1] n = 20, [2] n = 25;

[a] Backward regression analyses with SMR (only for the prediction model of TEE), weight (kg), height (cm), gender (1:boys, 2:girls), sleep (hours/day) and ACM or ACD as prediction factors. Entry criteria: 0.20, removal criteria: 0.25.

sleep duration explained 48% of the variance in PAL ($p = 0.033$), ACD, gender and sleep duration explained 39% of the variance in AEE ($p = 0.042$). The multivariate models predicting TEE with ACM and SMR or with ACD and sleep duration were not significant ($p = 0.053$ and $p = 0.103$). In figure 1 the regression lines of the backward regression models to predict PAL and AEE are shown.

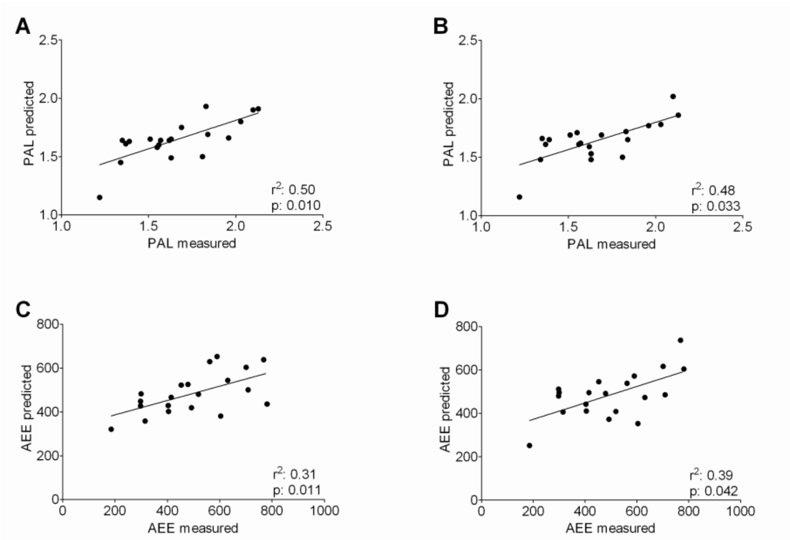

Figure 1. Measured versus predicted values for physical activity level (PAL) and activity energy expenditure (AEE). **A:** PALpredicted = 1.04 + 2.86*ACM*10^{-4} – 0.044*weight + 0.15*gender; **B:** PALpredicted = 0.265 + 4.24*ACD*10^{-7} – 0.011*height + 0.096*sleep duration + 0.195*gender; **C:** AEEpredicted = -189.8 +0.183*ACM; **D** AEEpredicted = -1411.6 + 2.93*ACD*10^{-4} + 2.8*sleep duration + 122.3*gender. ACD: activity counts per day, ACM: activity counts per minute, gender 1: boys 2: girls, height in cm, sleep duration in minutes, weight in kg.

We also evaluated whether TBW as an indicator of lean body mass was correlated with TEE. We found that TBW explained 36% of the variance in TEE. Adding the ACM, as measured with the activity monitor to the model, improved the explained variance to 43%.

Level of agreement in PAL between 5 and 3 days of predicted physical activity measures by the Tracmor$_D$ was assessed by using a Bland-Altman plot (Figure 2). PAL was predicted according to the equation PAL = 1.04 + 2.86*ACM*10^{-4} –

0.044*weight(kg) + 0.15*gender from Table 2. The difference in calculated PAL between 5 and 3 days wearing the accelerometer was not significant.

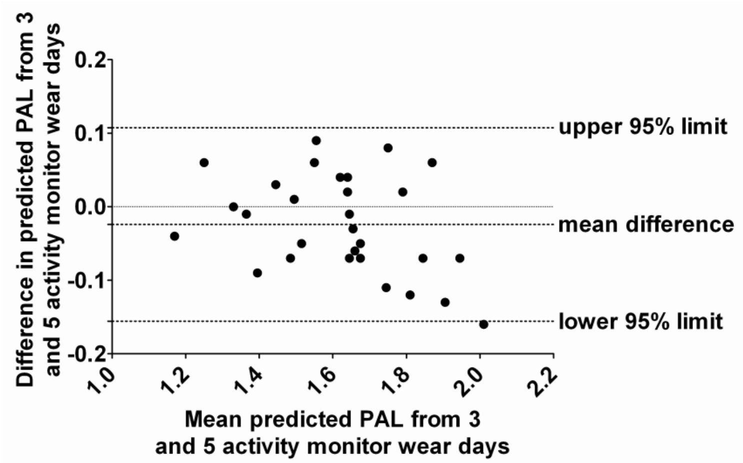

Figure 2. Bland-Altman plot for the level of agreement in predicted physical activity level (PAL) between 5 or 3 days of physical activity measurement by the TracmorD. Mean difference (bias): -0.02 ± 0.07 (-1.2% of mean PAL) and 95% limits of agreement of -0.16; 0.11 (-9.8; 6.8% of mean PAL).

DISCUSSION

The aim of this study was to test the validity evidence of the TracmorD to estimate energy expenditure used for free-living physical activity in preschoolers. The present study showed that the TracmorD provides moderate-to-strong validity evidence that supports its use to evaluate physical activity in this age group. Output of the TracmorD in ACM together with weight and gender gives a valid estimation of PAL, and ACM individually, gives a valid estimation of AEE. Output of the TracmorD in ACD together with height, gender and sleep duration gives a valid estimation of PAL and ACD together with gender and sleep duration of AEE. In our study the accelerometer was worn for 5 days, but we found 3 days of wearing the accelerometer did not gave a different estimated PAL.

In the univariate model ACM gave a higher explained variance than ACD, while in the multivariate model we found the opposite for the prediction of AEE. One of the differences in ACM and ACD is sleep duration. A higher sleep duration results in less wear time. Therefore two children with comparable ACM, but with different sleep duration could have different ACD. For the multivariate prediction models of PAL and AEE less prediction variables are needed when the ACM as outcome of the Tracmor$_D$ is used instead of the ACD. Above that the use of ACM needs no correction for non valid wear days. Therefore, for the prediction of PAL or AEE, ACM instead of ACD as output of the accelerometer might be more practical.

Tracmor$_D$ is validated before in adults (10). In that study weight and mean ACD explained 46% of the variance in AEE and mean ACD explained 46% of the variance in PAL. In a small group of children (n = 11) with a wide age range (3-11 years) an earlier version, the Tracmor2, was validated (11). This earlier version is of a larger size and weight and contains other sensors (9). Mean ACD predicted 62% of the variance in PAL (11). Few studies validated accelerometers in preschool children. Only Actical, Actiwatch and Actigraph were validated in children aged 2-5 years (24). In this age group only the CSA/MTI accelerometer (Actigraph) was validated against the DLW method to predict the AEE or the PAL. REE was estimated from the Schofield equation to calculate the PAL. In 104 children, mean age 5.5 years (range 2.6-6.9), accelerometer output (ACM) explained significantly 11% of the variance in PAL (25). In our study we found an explained variance of 31%. Different factors could contribute to this higher explained variance. First we used a tri axial instead of uni axial measurements. Secondly we measured on exactly the same days TEE by the DLW method and physical activity by the accelerometer, while Montgomery et al. did not (25). Finally REE was measured by the SMR from the ventilated hood instead of using the Schofield equation.

Important for the validation of the Tracmor$_D$ is that we used the gold standard for TEE, the DLW method, as reference method for TEE and we measured SMR by a ventilated hood instead of estimation of the REE according to the Schofield equation.

A first limitation of our study is the relatively small sample size with complete data. Secondly we measured SMR instead of BMR. BMR is the official variable used to calculate PAL from TEE. BMR is the resting, awake, thermo neutral, fasting energy expenditure. Children at this age are not willing to lay down for half an hour under a ventilated hood and fasting is a problem. Therefore, we replaced the BMR measurement by the 'evening' SMR measurement which was the best and most feasible option in children of this age category. Treuth (26) found a small, but not significant difference between the overnight SMR and the BMR, measured in the morning in 7-10 year old girls. We measured the

SMR rather soon after a meal, therefore it included also the diet induced thermogenesis. The SMR, as measured by us, might therefore be 5-10% higher than the BMR. Using the SMR in the early evening instead of the BMR might have given a small underestimation, but no overestimation of the PAL.

According to the FAO/WHO/UNU the PAL value in 3-4 year old children is 1.44. In our study PAL was 1.64. The FAO/WHO/UNU calculated PAL as TEE/$BMR_{estimated}$. The BMR estimation was based on the predictive equations on body weight according to Schofield (1985). Calculation of the BMR using the Schofield equation in our study gave a mean BMR of 860 kcal (results not shown). This is higher than the measured evening SMR, 765 kcal. When we calculated the PAL using the BMR estimated from the Schofield equation, the PAL is 1.46, what is almost equal to the PAL value given by the WHO: 1.44. Because of the lower value for the SMR, a higher value for the PAL was found. The most likely explanation is that the Schofield equation overestimates the BMR. When comparing the BMR estimated from the equation and our results, we found that the equation specially overestimates in the infants with a lower SMR. When looking at the Bland-Altman plot (results not shown) of the measured versus the estimated SMR/BMR we see that agreement is good at the higher levels of BMR/SMR. These children were the oldest and largest, and most close to the lower limit of age for which Schofield equation was developed, For younger children, we found that the lower the SMR, the larger the deviation between methods. Therefore, we believe that the discrepancy is due to the fact that BMR estimated according to the equation used by the FAO/WHO/UNU in this young age group may lead to errors, it may be less suitable for 3 to 4-year-old children. It is a well-known phenomenon that the error increases at the boundaries of the population for which the prediction equation was developed. The analyses for the prediction model of PAL and AEE contained significantly more girls than boys. We found no differences in the characteristics from Table 1 between boys and girls, therefore we do not expect that it influenced our results.

In conclusion, Tracmor$_D$ provides moderate-to-strong validity evidence that supports its use to evaluate PAL and AEE in preschool children. Wearing the accelerometer for 3 days is comparable to 5 days in this age group.

ACKNOWLEDGEMENTS

We thank the participants and their parents who participated in this study, Philips (Philips, DirectLife, The Netherlands) for providing the TracmorD instruments and Rotterdam Erasmus MC for performing the DLW analyses of the saliva samples.

AS participated in the study design, carried out measurements, analyzed data and wrote the manuscript. HS analyzed the DLW samples and provided writing assistance. AG and KJ provided instruments, technical support and writing assistance. IK participated in the study design. EC and PS participated in the study design and in the interpretation of the data and critically supervised writing of the manuscript.

DISCLOSURE

The accelerometers used were provided by Philips DirectLife, The Netherlands

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Chapter 6

Infant movement opportunities are related to early growth – GECKO Drenthe cohort

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Early Human Development 2013, in press

ABSTRACT

BACKGROUND: Movement by an infant during the first year of life might influence its activity level and thereby influence growth in early childhood.
AIM: To examine whether the time that an infant is able to move unrestrictedly and time spent in baby seats are related to weight and waist circumference at age 9 months and growth from 9 to 24 months.
METHODS: In the GECKO Drenthe birth cohort, weight and height were measured in Well Baby Clinics at the ages of 9 and 24 months. Time spent moving unrestrictedly and time spent in baby seats were reported on a questionnaire at age 9 months. Children born <37 weeks or with a low birthweight (<2500 g) were excluded. Outcomes were defined as the Z-scores for weight-for-height, weight-for-age, and waist circumference-for-age at the ages of 9 and 24 months, and changes in Z-scores as between 9 and 24 months of age.
RESULTS: The time an infant is able to move unrestrictedly at age 9 months was inversely related to Z-score waist circumference at 9 months, and the change in Z-scores weight-for-height and weight-for-age between the ages 9 and 24 months. For time spent in baby seats, 'never users' showed a decline in Z-score weight-for-height as compared to those who used baby seats. On the contrary, Z-score waist circumference-for-age declined in children sitting for 1 hour or more in baby seats.
CONCLUSION: More time spent moving unrestrictedly in infancy may contribute to a healthy growth pattern.

INTRODUCTION

In 2010, the prevalence of obesity was estimated to be 11.7% in children aged 0-5 years in developed countries (1). These children have a substantially increased health risk (2-4). Rapid increases in weight and BMI during infancy are related to an unhealthy growth pattern and are associated with increased risk of being overweight in childhood (5). Furthermore childhood overweight is associated with overweight and obesity in adulthood (6). Once overweight, it is hard to become and to stay lean. Therefore, prevention of overweight and stimulation of healthy growth at a young age may well reduce the obesity problem.

Already in early childhood, physical activity may be protective against the development of overweight (7,8). Better movement skills may encourage physical activity through improved self-confidence and enjoyment of physical activity. Children with reduced skills will engage in less physical activity (9-11), which increases the risk of overweight (12). Avoiding physical activity also results in a lack of movement experiences and inhibits further motor development. Therefore, children with an inactive lifestyle at a young age may find themselves in a vicious circle. The foundation for these movement skills are basic movement patterns developed during early postnatal ages (13,14). Thus, already during infancy, motor development may be important for subsequent physical activity. Physical inactivity at a young age results in a lack of movement experience which may also lead to poor development of the basic movement patterns. This can partly be a reflection of a genetic predisposition, resulting in a physically active child due to natural aptitude (11). In addition, it is assumed that parental care-giving practices can influence basic movement patterns in infants (15,16). For example, at age 4 and 6 months more time spent in a prone position while awake is associated with a higher motor development score (16). Other care-giving practices that could influence physical activity and thereby the development of overweight may be the use of baby seats and free moving time. When infants are placed in baby seats or baby carriers for a longer period of time, their physical activity may be restricted. On the other hand, being able to move in an unrestricted way, for example, in a playpen or on a carpet, may directly encourage a child's physical activity and thus stimulate motor development. Moreover, more physical activity may positively influence the amount of fat-free body mass and may result in a more healthy growth pattern.

To the best of our knowledge, no study has examined the relationship between an infant's being able to move unrestrictedly and time spent in baby seats in relation to weight or weight gain at very young age. The aim of this prospective study is to examine whether the time an infant is able to move unrestrictedly and time spent in baby seats are related to weight and waist circumference at age 9 months and growth between 9 and 24 months.

METHODS

Subjects

This study was performed using GECKO (Groningen Expert Center for Kids with Obesity) Drenthe birth cohort data (17). All children who were born between April 2006 and April 2007, and were at time of birth living in the Province of Drenthe (the Netherlands) were asked to participate in the GECKO Drenthe cohort. Data collection began during the last trimester of pregnancy. Neonatal and childhood data were obtained during regular visits to the Well Baby Clinics. Within the Dutch Health Care system, Well Baby Clinics occupy a central position during the first four years of life. Written informed consent was obtained, and the study was approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG).

Inclusion and exclusion criteria

All children participating in the GECKO Drenthe birth cohort for whom sufficient data was available were included. The exclusion criteria for this study entailed those born before 37 weeks of gestation or those with low birthweight (<2500g).

General characteristics

Date of birth, gender, birthweight, and gestational age were reported by midwives shortly after birth and by the parents in a questionnaire within 2 months after birth. When a discrepancy between the responses of parents and midwives was found, the responses of the midwives were selected.

Anthropometric measurements

At age 9 months and at age 24 months, weight, height, and waist circumference were measured by trained nurses at the Well Baby Clinics. If the anthropometric measurements at 9 or 24 months were missing, and the measurements before and after 9 or 24 months were available (6 or 7 and 11 or 14 months; 14 or 18 and 36 of 45 months, respectively), the anthropometric measurements for 9 and 24 months were estimated by interpolation. At all visits, body weight was measured in light clothing using an electronic scale with a digital display, which recorded to the nearest 0.01 kg. Length at 9 months was assessed using an infantometer and at 24 months by using a stadiometer, and recorded to the nearest 0.1 cm. Waist-circumference measurement was performed with a standard tape measure and recorded to the nearest 0.1 cm, at 9 months in supine, and at 24 months in standing position. Waist circumference was measured at the mid-point between the lower costal margin and the level of the anterior superior iliac spine. Z-scores weight-for-height, weight-for-age, and waist circumference-for-age within the GECKO Drenthe cohort were calculated by gender. Growth between 9 and 24 months was determined from the Z-scores weight-for-height, weight-for-age, and waist circumference-for-age at 24 months minus the Z-scores at 9 months.

Time in baby seats and unrestricted moving time

At the age of 9 months parents were asked in a questionnaire to report how many hours per day their child spent in baby seats: never, <1 hour, or ≥1 hour per day ("How many hours per day is your child sitting in a car seat or child seat?"). We also asked how many hours their children were able to move unrestrictedly ("How many hours per day is your child able to move freely, for example, on a carpet or in a playpen?"). Being able to move unrestrictedly was analyzed both as a variable at ratio level (total unrestricted moving time) and as a dichotomous variable (<5 hours or ≥5 hours unrestricted moving time per day). The cut-off point was based on the median of unrestricted moving-time hours. Children were divided into 4 profiles from most to least restricted: 1, ≥1h in baby seats, <5h unrestricted moving time, as long time in baby seats and short time in unrestricted moving; 2, <1h in baby seats, <5h unrestricted moving time, as short time in baby seats and short time in unrestricted moving; 3: ≥1h in baby seats, ≥5h unrestricted moving time, as long time in baby seats and long time in unrestricted moving; 4, <1h in baby seats, ≥5h unrestricted moving time, as short time in baby seats and long time in unrestricted moving

There is no standard definition for unrestricted moving. Unrestricted moving can be defined as the time a child is able to be spontaneously active in the way the child wants to be, or when the physical activity is not restricted by physical constraints.

Statistical analyses

The mean and the 95% range were calculated for all characteristics. Differences in baseline characteristics of the children included and of the children not in the analysis were tested using an independent Student's t-test. Gender differences in unrestricted moving time or time in baby seats were tested using the independent Student's t-test and chi-square test. The association between time in baby seats and unrestricted moving time was tested using ANOVA; a post hoc analysis was done using a Bonferroni correction. An independent Student's t-test was used to test differences between the two groups of unrestricted moving time in Z-score weight-for-height, Z-score weight-for-age, and Z-score waist circumference-for-age. An ANOVA was used to test significant differences between the three groups for time in baby seats in terms of Z-score weight-for-height, Z-score weight-for-age, and Z-score waist circumference-for-age. A post hoc analysis was done using a Bonferroni correction. To calculate the difference in weight-for-height, weight-for-age and waist circumference-for-age Z-scores between children who were most and least restricted in their physical activity, we performed an independent Student's t-test between children with profile 1 (most restricted) and profile 4 (least restricted). P values of 0.05 or less were considered to indicate statistical significance. All statistical analyses were performed using PASW statistics version 18.

RESULTS

Almost 50% of the participants in the GECKO Drenthe cohort study could not be included in this study due to missing data. Informed consent was obtained for 2997 children, 2418 of whom met the inclusion criteria. The questionnaire was missing for 575 children, because parents stopped participating or did not fill in the questionnaire. Of the 1843 remaining children, some children did not visit the Well Baby Clinic at the time points we required for our study, or they had no registration for anthropometric measurements at these time points, had incomplete records from the Well Baby Clinics, or the anthropometric measurements were not sent out properly by the Well Baby Clinics via mail. We analyzed the cross-sectional data in 1722 children and the prospective data in 1283 children. The children with incomplete data were comparable in gender, birthweight, and gestational age to those who were included in this study at age 9 months and at age 24 months. Children who had incomplete data at 24 months, but were included at 9 months, did not differ in anthropometric measurements, unrestricted moving time, or time in baby seats at age 9 months as compared to those children who were included at 24 months. The characteristics of the included subjects are shown in Table 1. Mean weight and height was 9.2±1.0kg and 73.0±2.6cm, respectively, at 9 months of age, and 13.1±1.5kg and 89.6±3.4cm, respectively, at 24 months of age. Mean unrestricted moving time was 4.5±2.3 hours/day. Sixty-three children (4%) never used baby seats, 1425 children (83%) used baby seats for less than 1 hour per day, and 226 children (13%) used baby seats for 1 hour or more per day. No differences in unrestricted moving time or time in baby seats were found between boys and girls. Less time in baby seats was associated with more unrestricted moving time ($p = 0.02$). In a post hoc analysis, the group who never used baby seats had significantly more unrestricted moving time than the ≥1hour baby seat group (5.0±3.3 and 4.1±2.0 hours, respectively, $p = 0.03$). Children were divided into 4 profiles: profile 1, n = 142 (8%) at age 9 months and n = 102 (8%) at age 24 months; profile 2, n = 851 (50%) at age 9 months and n = 632 (50%) at age 24 months; profile 3, n = 82 (5%) at age 9 months and n = 64 (5%) at age 24 months; profile 4, n = 635 (37%) at age 9 months and n = 474 (37%) at age 24 months.

Table 1. Characteristics of the subjects at 9 and 24 months

	Age 9 months		**Age 24 months**[a]	
	mean±SD	**95% range**	**mean±SD**	**95% range**
Boys/Girls (n)	880/842		655/628	
Birthweight (grams)	3609±489	2806-4474	3608±497	2802-4499
Gestational age (weeks)	40±1.3	38-42	40±1.3	38-42
Age (weeks)	41±2.4	37-45	110±6	103-121
Weight (kg)	9.2±1.0	7.7-10.9	13.1±1.5	10.8-15.7
Height (cm)	73.0±2.6	69.0-77.4	89.6±3.4	84.0-95.0
Waist circumference (cm)	43.4±3.2	38.0-45.5	47.5±3.1	42.7-53.0
Weight-for-height (kg/m)	12.6±1.1	10.9-14.5	14.7±1.3	12.6-16.9
Weight-for-age (kg/yr)	11.8±1.3	9.8-14.1	6.2±0.7	5.2-7.4
Waist circumference-for-age (cm/yr)	55.6±5.2	47.0-64.4	22.5±1.8	19.7-25.5
Time in baby seats (hours)	1.1±0.5	1.0-2.0		
Unrestricted moving time (hours)	4.5±2.3	2.0-8.0		

SD: standard deviation

[a] No significant differences between the characteristics of the drop-out and follow-up groups.

Weight and waist circumference at age 9 months

At the age of 9 months, a small but significant inverse association between total unrestricted moving time and the Z-score waist circumference-for-age ($B = -0.02$, $p = 0.03$) was observed. When we divided unrestricted moving time into two groups based on the median (<5 hours and ≥5 hours), no significant differences were found in Z-scores weight-for-height, weight-for-age, or waist circumference-for-age (Table 2). Time in baby seats was divided into three groups, that is, never, <1hour, and ≥1hour. Among these 3 groups for time in baby seats, no significant differences in Z-score weight-for-height, weight-for-age, or waist circumference-for-age were found (Table 3). At the age of 9 months no differences in weight-for-height, weight-for-age and waist circumference-for-age Z-scores between children with profile 1 (most restricted) and profile 4 (least restricted) were found.

Table 2. Z-scores weight-for-height, weight-for-age, and waist circumference-for-age at 9 and 24 months of age in relation to < 5 hours and ≥ 5 hours unrestricted moving time at 9 months of age (mean±standard deviation).

	Unrestricted moving time	**9 months[a]**	**24 months[a]**	**Δ 9-24 months[b]**
Weight-for-height	<5 hours	0.04±0.97	0.04±0.98	0.04±0.80
Z-score	≥ 5 hours	0.06±1.01	-0.02±0.99	-0.11±0.70**
Weight-for-age	<5 hours	0.06±0.95	0.06±0.97	0.02±0.79
Z-score	≥ 5 hours	0.04±1.02	-0.01±1.02	-0.08±0.76*
Waist circumference-for-age	<5 hours	0.04±0.99	0.03±0.97	-0.02±1.14
Z-score	≥ 5 hours	-0.05±1.01	0.00±1.01	0.01±1.13

Significant differences between the 2 groups of unrestricted moving time: * $p < 0.05$; ** $p < 0.01$.

[a] n=1722 for the total group (58% <5h group)

[b] n=1283 for the total group (58% <5h group)

Growth from 9 to 24 months of age

Total unrestricted moving time was significantly inversely associated with a change in Z-score weight-for-height (B = -0.03, p = 0.001). In Table 2, the Z-scores weight-for-height, weight-for-age, and waist circumference-for-age for the groups <5 hours and ≥5 hours of unrestricted moving time are shown. Children who had <5 hours of unrestricted moving time increased in terms of their Z-score weight-for-height and Z-score weight-for-age. On the other hand, those who had ≥5 hours of unrestricted moving time decreased their Z-score weight-for-height and Z-score weight-for-age. The change in Z-score weight-for-height and Z-score weight-for-age was significantly different between the two groups (p<0.001 and p = 0.02, respectively). For waist circumference-for-age, no significant differences in Z-scores were found.

In Table 3 differences in Z-score weight-for-height, weight-for-age, and waist circumference-for-age in relation to time in baby seats is shown. Less time in baby seats was significantly associated with a higher decrease in Z-score weight-for-height ($p = 0.03$) and Z-score weight-for-age ($p = 0.02$). A post hoc analysis for Z-score weight-for-height showed that this significant association was mainly due to the "never users"; post hoc weight-for-age was no longer significant. Children of parents who reported never using baby seats at 9 months of age showed a decline in Z-score weight-for-height and Z-score weight-for-age when compared to those who used baby seats. It should be noted that these children showed non-significant higher Z-score values at 9 months. With Z-score waist circumference-for-age, we found that more time in baby seats was associated with a decrease in Z-score waist circumference-for-age ($p = 0.03$), and that this difference was mainly present in those who used baby seats for ≥1 hour when compared to the <1 hour group.

Table 3. Z-scores weight-for-height, weight-for-age, and waist circumference-for-age at 9 and 24 months of age between never, <1 hour, and ≥1 hour time in baby seats at 9 months of age (mean±standard deviation).

	Time in baby seats	**9 months[a]**	**24 months[b]**	**Δ 9-24 months[b]**
Weight-for-height	Never	0.28±1.06	-0.02±1.05	-0.34±0.63
Z-score	< 1 hour	0.04±0.98	0.02±0.98	-0.02±0.77[c]
	≥1 hour	0.02±1.01	-0.06±1.03	0.00±0.71*[c]
Weight-for-age	Never	0.31±1.05	0.12±1.01	-0.30±0.82
Z-score	< 1 hour	0.03±0.98	0.04±1.00	0.00±0.78
	≥1 hour	0.07±0.98	-0.11±0.92	-0.11±0.74*
Waist circumference-for-age	Never	0.10±1.09	0.17±0.91	0.00±1.26
Z-score	< 1 hour	-0.02±1.00	0.04±1.00	0.03±1.15
	≥1 hour	0.07±0.97	-0.19±0.90**[d]	-0.22±1.04*[e]

Significant differences between the time in baby seat groups from ANOVA: * $p < 0.05$; ** $p < 0.01$.

[a] n=1714 for the total group (never 4%; <1 hour 83%; ≥1 hour 13%)

[b] n=1276 for the total group (never 3%; <1 hour 84%; ≥1 hour 13%)

Post hoc analyses:

[c] $p<0.05$ for never vs. <1h and never vs. ≥1h

[d] $p<0.05$ for <1h vs. ≥1h

[e] $p<0.05$ for <1h vs. ≥1h

We divided the children into different profiles. Between the age of 9 and 24 months weight-for-height Z-score increased in children with profile 1 (most restricted) and 2 and decreased in children with profile 3 and 4 (least restricted) (change in Z-score: 0.016, 0.04, -0.05 and -0.12, respectively, $p = 0.004$). For waist-circumference-for-age we found the opposite. Children in profile 4 (least restricted) increased their in waist circumference-for-age Z-score, while children in profile 1 (most restricted) decreased their waist circumference-for-age Z-score between the age of 9 and 24 months (change in Z-score = 0.05 and -0.21, respectively, $p = 0.03$).

DISCUSSION

In this study we found a small but significant inverse relationship between the time an infant is able to move in an unrestricted way at age 9 months and waist-circumference at 9 months, and the change in weight-for-height and weight-for-age from age 9 to 24 months. Therefore, we suggest that more time in which an infant has the option to move unrestrictedly may contribute to a healthy growth pattern. Children whose parents never used baby seats declined more in terms of Z-score weight-for-height and weight-for-age compared to those whose parents did use baby seats. On the other hand, Z-score waist circumference-for-age declined in children sitting for 1 hour or more in baby seats.

The increase in childhood obesity has become a great concern, and one of the factors that has been mentioned is the level of physical activity. We hypothesized that the use of baby seats and limited time to move unrestrictedly may be related to the development of weight over time, since use of baby seats and time to move unrestrictedly are likely to be determinants of the level of physical activity, both directly and indirectly via development of motor skills. Previous studies in infants found an inverse relationship between physical activity level and percentage of body fat (18,19). In infants it may not be easy to increase the amount of physical activity, but more time to move unrestrictedly (e.g., on a carpet or in a playpen) might be a practical way to stimulate infants in order to increase their physical activity and provide them with the option of increasing their motor experiences. In the literature we found no studies that investigated the relationship between the option of moving unrestrictedly and growth. Of the prospective studies examining the relationship between measured physical activity and growth, Wells and colleagues found a positive relationship between infant time spent quietly at age 9-12 months and childhood skin folds at age 24 months, whereas infant time spent actively was inversely related (7). Opposite results were found in another study including younger infants: Low activity levels in early infancy (at least at 6 months of age) were not a good predictor of fatness at age 12 months (19). Our results showed that more time to move unrestrictedly was related to a smaller increase in weight-for-height and weight-for-age. Although the effects were modest, this supports the idea that the option of moving unrestrictedly is beneficial for a healthy growth pattern.

No studies had ever evaluated the effect of restriction in activity due to the use of baby seats on growth in young infants. Parents of most children (84%) used baby seats for less than 1 hour/day. Only few children (4%) were never-users or used the baby seats for more than 1 hour/day (13%). The never-users tended to decline more in weight-for-height and weight-for-age than children of parents who did use baby seats. The benefits for never-users appear to be related to the higher weight-for-height and weight-for-age Z-scores at baseline. At 24 months, the weight-for-height and weight-for-age Z-scores are almost the same in all three groups; therefore, in never-users the decline was steeper. On the other hand, Z-score waist circumference-for-age declined for those children who spent the most time in baby seats. The never-users did not differ in terms of having a car, mean income, and mean sleep time from the users, but they did differ in that more often their parents were unemployed (data not shown). This could have influenced the results, because a low socioeconomic status results in a higher risk for overweight, even as early as during the first months of life (20). Another factor influencing the results is the Dutch recommendation concerning the use of baby seats. In the Netherlands, it is recommended that baby seats not be used more than 2 hours a day. Only 5 children (0.3%) spent more than 3 hours a day in a baby seat. Most people acted upon the recommendation. This might have caused a ceiling effect. Because of the small effects, in combination with the low amount of children in the never-users and the ≥1 hour group, as well as the small range of time in baby seats, we cannot conclude whether and how time in baby seats affects the growth pattern.

This study has some strengths and limitations. Due to incomplete data, a considerable amount of cases were not able to be included in the analysis. At the same time, the baseline characteristics of those included and not included were comparable; the group that was examined for analysis was still quite large. Furthermore, our study is unique in that it investigates the association of being able to move unrestrictedly and being restricted in activity by the use of baby seats with growth at this young age. Another limitation in our study is that we did not objectively measure physical activity in the infants, but used only subjective parental report of the unrestricted moving time. Further studies are needed to investigate whether the associations found in this study persist into later age. Furthermore, it would be interesting to identify the determinants of the level of physical activity at this young age, and prospectively assess its relationship to growth.

In conclusion, more time made available to move unrestrictedly in infancy may contribute to a healthy growth pattern. Furthermore, there is no reason to believe that the use of baby seats for less than two hours per day has any adverse effect on the development of weight in young children.

ACKNOWLEGDEMENTS

We would like to thank the children and their parents who participated in this study and the staff of the Children's Health Clinic (Icare Foundation) for measuring the children.

CONFLICTS OF INTEREST

The authors declare there are no competing interests in relation to the work described.

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Chapter 7

Television time, sleep duration, outdoor play and BMI in young children: GECKO Drenthe cohort

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ABSTRACT

OBJECTIVE: Recent evidence shows that childhood overweight develops between 2 and 6 years of age, and prevention strategies in the first years of life deserve more attention. The aim of this study is to investigate the interplay between screen time, sleep duration, outdoor play, having a television in the bedroom and the number of televisions at home and their association with BMI in 3- and 4-year-old children.
METHODS: All participants, (3-4 years, n=759), were part of the GECKO Drenthe birth cohort. Weight and height were measured according to a standardized protocol by trained nurses. Lifestyle related behaviour, total screen time, number of televisions at home, a television in the bedroom, sleep duration and time of outdoor play were self-reported by parents in a questionnaire. OLS regression-based path analysis was used to estimate direct and indirect effects on BMI in mediation models.
RESULTS: A television in the bedroom or more televisions at home gave a higher screen time, which in turn decreased the sleep duration and resulted in higher BMI (indirect effect=0.0115, 95% bootstrap interval=0.0016; 0.0368 and indirect effect=0.0026, 95% bootstrap interval=0.0004; 0.0078, respectively). In contrast to the direct effect of screen time, sleep duration and a television in the bedroom on BMI, no direct effect was found for outdoor play and number or televisions at home on BMI.
CONCLUSION: Short sleep duration, long screen time, and a television in the bedroom contribute to the presence of overweight in children aged 3 and 4 years.

INTRODUCTION

Not only in adults, but also in young children the prevalence of overweight and obesity has been increasing rapidly during the last decades (1,2). Obesity causes general health risks on individual level (3) and on economic level an increase in the health care costs (4). Recent evidence shows that childhood overweight develops between 2 and 6 years of age (5,6), and prevention strategies in the first years of life deserve more attention (7-9). To prevent overweight in adolescence and adulthood, detection and treatment of overweight and obesity already in the first years of life is necessary. In adults, the intake of energy dense food, often cheap and available everywhere, other unhealthy eating habits, a low amount of physical activity, sedentary behaviour and sleep deprivation are associated with the development of obesity (10,11). In children, especially young children, the home environment is important for providing a healthy lifestyle. Parents give their children the opportunity to play outside, decide the duration of watching television and can affect their children's sleeping patterns.

Several previous studies discuss behaviours that correlate with overweight in preschool as well as in school-aged children (12-15). These behaviours include a lack of outdoor play, short sleep duration and sedentary behaviour, like watching television. Excess time in watching television may limit the time an infant sleeps (16-18), but no relation between watching television and outdoor play was found (19-21). Playing outside can be protective for the development of overweight (22), but this was not found in all studies (19,23). Studies in children younger than 5 years, evaluating the association of sleep duration, television time, number of televisions, a television in the bedroom and outdoor play with overweight, focused mainly on one or two aspects at the time. The interrelationships of these factors were not evaluated, although these factors may have complex interactions. Sleep duration may be a mediator in the relation between watching television, outdoor play and BMI. More outdoor play and less television time may be associated with a better and longer sleeping pattern. Better quality and quantity of sleep may in turn help to prevent adverse eating behaviours.

Therefore, the aim of this study is to investigate the interplay between screen time, sleep duration, outdoor play, having a television in the bedroom and the number of televisions at home and their association with BMI in 3- and 4-year-old children.

MATERIAL AND METHODS

Subjects

All children, 3 and 4 years of age, were participating in the GECKO Drenthe birth cohort. The GECKO Drenthe study is a population based birth cohort studying early risk factors for overweight and obesity in children living in Drenthe, a northern province of The Netherlands. Details of the study design, recruitment and study procedures were described in detail elsewhere (24). At baseline, parents of 2997 children intended to participate in the study, of whom 2874 ever actively participated. At the child's age of 3 or 4 years, complete data on weight, height, and questionnaires on environmental factors was available from 759 children. Data was collected from 2009 to 2011. Missing data could mainly be attributed to logistic and organizational problems. For all children, written informed consent was obtained from parents, and the study was approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG).

Anthropometric measures

At the age of 3 or 4 years children were measured by trained nurses at the Well Baby Clinics. Weight was measured in light clothing using an electronic scale with digital reading, and recorded to the nearest 0.1 kg. Height was assessed using a stadiometer and recorded to the nearest 0.1 cm. BMI was calculated as weight/height^2.

Lifestyle related behaviours

In the same time period as the anthropometric measures, parents were asked to fill in a questionnaire about lifestyle related behaviours of the child, which was provided by the Well Baby Clinic Nurse. The questions: 'Does your child has a television in his/her bedroom?' (yes/no) and 'How many televisions are present at home' (0, 1, 2 or >2) were asked. Parents were asked for how many days; and the average time per day (never, 0-½ hour, ½-1 hour, 1-2 hours, >2 hours) their child watches television, plays computer games and plays outdoor, separate for week and weekend days. To make one outcome for television time, one for computer time and one for outdoor play time, the use of the categories was not suitable. To make a total mean score, reflecting average television time, computer time and outdoor play time per day, the categories were translated to time in minutes to calculate mean time in minutes per day for each child separately: never = 0 minutes, 0-½ hour = 15 minutes, ½-1 hour = 45 minutes, 1-2 hours = 90 minutes and >2 hours = 180 minutes. Mean times per day watching television, playing computer games or playing outdoor were calculated over the whole week (including both week and weekend days). Because the time spent on computer games was minimal, total screen time per day was calculated as the sum of the time watching television per day and the time playing computer games per day. Finally bedtimes and wake times were reported, separate for week and weekend days. Mean sleep time per night in minutes was calculated.

Statistics

All children participating in the GECKO Drenthe birth cohort with sufficient data available were included. Data are presented as mean±SD, and range (min-max). Groups were compared by Student's T-test or One-way ANOVA and associations by Pearson correlations. In the Post Hoc test a Bonferroni correction was made. OLS (ordinary least square) regression-based path analysis was used to estimate direct and indirect effects (path coefficients (unstandardized B)) on BMI in mediation models with the PROCESS macro for SPSS. (Hayes, 2012, http://www.afhayes.com/). Model 1 is a mediation model with screen time as dependent variable, sleep duration as mediator, BMI as outcome variable and gender as covariate. In model 2a the dependent variable, television in the bedroom (0: no, 1: yes), is added. In model 2b the dependent variable, number of televisions at home (1: ≤1 TVs, 2: 2 TVs, 3: >2 TVs), is added. In both model 2a and 2b screen time and sleep duration were mediators, BMI was the outcome variable and gender was the covariate. For the indirect effects 10 000 bootstrap samples were used for bias corrected bootstrap confidence intervals. Screen time and outdoor play tended to deviate from normal distribution, but when included in the regression-based path analysis the residuals were normally distributed, so the model assumptions were not violated by this. Statistical analyses were performed using PASW 18.0.3 for Windows (SPSS, Chicago Illinois, USA). The significance level was set to $p < 0.05$ (2-tailed).

RESULTS

First we analyzed whether BMI was different for children with or without a questionnaire. Mean BMI was significantly different between children with or without a questionnaire (15.7 and 15.9, respectively $p = 0.02$), but the ranges were approximately equal and no significant difference in the percentage of children with overweight or obesity was found, making systematic bias due to missing vales from questionnaire data unlikely. From all children with questionnaire data, screen time was missing in 8 (1%) children and sleep duration in 4 (<1%) children.

In table 1, characteristics of the children are shown. Fifty-three percent were boys. Nine percent were overweight and 2% were obese. The children had a mean screen time of 61±40 minutes per day, mostly from watching television. At this young age, 15 children (2%) played computer games for more than 30 minutes, of whom only 4 played more than 1 hour, and 557 children (73%) never played computer games. Children slept on average 11.7±0,5 hours per day and played outdoors for 94±52 minutes per day. Twenty-five (3.3%) children had a television in their bedroom. Four (<1%) children had no television present in their home, 209 children (28%) had 1 television, 419 (55%) children had 2 televisions and 127 (17%) children had more than 2 televisions in their home. No or 1 television at home was combined as one group.

Table 1. Characteristics of the children

	N (%)
N	759
Boys	401 (53)
Overweight (excl. obese)[1]	66 (9)
Obese[1]	12 (2)
TV in bedroom	25 (3)
≤1 TVs at home	213 (28)
2 TVs at home	419 (55)
>2 TVs at home	127 (17)
	Mean ± SD and range (min-max)
Age (years)	3.9 ± 0.1 (3.4 - 4.4)
Weight (kg)	17.5 ± 2.2 (11.3 - 29.8)
Height (m)	1.05 ± 0.04 (0.91 - 1.19)
BMI (kg/m²)	15.7 ± 1.3 (12.6 - 21.8)
TV time (min/day)	58 ± 38 (0 -180)
Computer time (min/day)	3 ± 9 (0 -90)
Screen time (min/day)	61 ± 40 (0 - 225)
Sleep duration (min/day)	701 ± 30 (591 - 810)
Outdoor play (min/day)	94 ± 52 (0 - 180)

[1] Overweight and obesity classification according to Cole et al. (25)

In our study, screen time, outdoor play and sleep duration were reported by the parents separately for week and weekend days. Sleep did not differ between week and weekend days. Outdoor play and screen time did differ between week and weekend days, for outdoor play 88.8±53.3 and 105.5±61.3 minutes, respectively and for screen time 58.3±41.6 and 67.1±46.9, respectively. In the analysis, we were interested in the total screen time, outdoor play and sleep duration per week, so we analyzed the mean time per day over the week without distinguishing between week and weekend days.

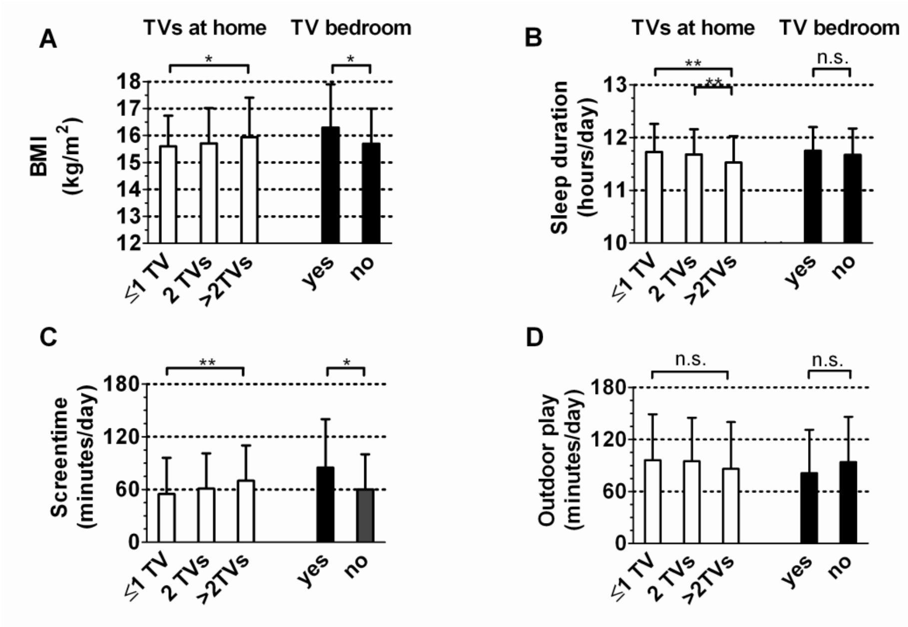

Figure 1. Number of televisions at home and a television in the child's bedroom versus BMI (A), sleep duration (B), screen time (C) and outdoor play (D). Number of televisions at home: ≤1 TV, n = 213 (28%); 2 TVs, n = 419 (55%); >2 TVs, n = 127 (17%) Television in bedroom: yes, n = 25 (3%); no, n = 734 (97%)

* P < 0.05; ** P < 0.01

In figure 1, differences in BMI (A), sleep duration (B), screen time (C) and outdoor play (D) between the children with ≤1 television, 2 televisions and >2 televisions at home are shown. For children with ≤1 television, 2 televisions and >2 televisions, BMI was 15.6±1.1, 15.7±1.3, and 16.0±1.5 kg/m^2, respectively (≤1 TV vs. >2 TVs p = 0.046). Screen time was 55±41, 61±40, and 70±40 minutes/day, respectively ((≤1 TV vs. >2 TVs p = 0.004). Sleep duration was 704±32, 701±29, and 692±30 minutes/day, respectively (≤ 1 TV vs. >2 TVs p=0.001, 2 TVs vs. >2TVs p = 0.006). Outdoor play time was 96±53, 95±50, and 86±54 minutes/day, respectively (n.s.). In figure 1, also the differences in BMI, sleep duration, screen time, and outdoor play between the children with a television in the bedroom and no television in the bedroom are shown. For a television in the bedroom versus no television in the bedroom, BMI was 16.3±1.6, and 15.7±1.3 kg/m^2, respectively ($p = 0.021$). Screen time was 85±55, and 60±40 minutes/day, respectively ($p = 0.035$). Sleep duration was 705±27, and 700±30 minutes/day, respectively (n.s.). Outdoor play time was 81±50, and 94±52 minutes/day, respectively (n.s.).

In table 2, the correlations between BMI, screen time, sleep duration and outdoor play are shown. Longer screen time ($p = 0.006$) and shorter sleep duration ($p = 0.003$) were associated with a higher BMI. Longer screen time was also associated with less outdoor play ($p = 0.006$) and a shorter sleep duration ($p < 0.001$).

Table 2. Pearson correlation coefficients of BMI, screen time, sleep duration and outdoor play.

	BMI		**Outdoor play**		**Sleep duration**	
	r	**p**	**r**	**p**	**r**	**p**
Screen time (min/day)	**0.101**	**0.006**	**-0.101**	**0.006**	**-0.156**	**<0.001**
Sleep duration (min/day)	**-0.108**	**0.003**	0.060	0.101	-	-
Outdoor play (min/day)	-0.010	0.794	-	-	-	-

Bold printed coefficients are significant.

To further investigate the interrelationships, the independent associations of the direct and indirect relationships were analyzed in 3 path coefficients models (table 3). The given path coefficients are shown as unstandardized B. In model 1, as explained in the statistics, both the direct effect of screen time on BMI ($c' = 0.0027$, $p = 0.024$) and the indirect effect via sleep duration ($a_1b_1 = 0.0004$, 95% bootstrap interval = 0.0001; 0.0010) were significant (table 3). Thus, firstly 1 hour (60 minutes) of more screen time is directly associated with a higher BMI of 0.0027*60 = 0.16 kg/m^2. And additionally, 1 hour (60 minutes) of more screen time is associated with less sleep duration of 60*0.1153 = 7 minutes. And these 7 minutes of lower sleep duration are associated with 7*0.0038 = 0.03 higher BMI. Total effect: 1 hour extra screen time gives a higher BMI of 0.03+0.16 = 0.19 kg/m^2. Figures 2 and 3 show the more complex serial multiple mediator models 2a and 2b. In model 2a and 2b, all separate pathways were significant, except for a television in the bedroom with sleep duration in model 2a (figure 2) and the direct effect of number of televisions on BMI in model 2b (figure 3). In model 2a we found that children with a television in their bedroom have a higher BMI than children with no television in their bedroom (direct effect = 0.5547, 95%CI = 0.0748; 1.1120) and two of the 3 indirect effects were significant (table 3). A television in the bedroom gave a higher screen time, which in turn decreased the sleep duration and resulted in higher BMI (indirect effect = 0.0115, 95% bootstrap interval = 0.0016; 0.0368). In model 3 we found no direct effect of the number of televisions on BMI, but all 3 indirect effects were significant (table 3). More televisions increased the screen time, which in turn decreased the sleep duration and resulted in a higher BMI (indirect effect = 0.0026, 95% bootstrap interval = 0.0004; 0.0078). The models that included outdoor play were not shown. Outdoor play had no effect on BMI in both direct and indirect pathways.

Table 3. Path coefficients of lifestyle factors associated with BMI.

Path	Path coefficients [95% CI] model 1	Path coefficients [95% CI] model 2a[1]	Path coefficients [95% CI] Model 2b[2]
TV → BMI	n.a.	**0.5547 [0.0784; 1.1120]**	0.1320 [-0.0105; 0.2745]
TV → screen	n.a.	**24.6976 [8.5287; 40.6666]**	**7.2010 [2.8045; 11.5974]**
TV → sleep	n.a.	7.5731 [-4.2991; 19.4454]	**-4.8996 [-8.1377; -1.6614]**
Screen → sleep	**-0.1153 [-0.1679; -0.0627]**	**-0.1190 [-0.1719; -0.0661]**	**-0.1060 [-0.1586; -0.0533]**
Screen → BMI	**0.0027 [0.0004; 0.0050]**	**0.0024 [0.0001; 0.0047]**	**0.0025 [0.0001; 0.0048]**
Sleep → BMI	**-0.0038 [-0.0069; -0.0006]**	**-0.0039 [-0.0071; -0.0008]**	**-0.0035 [-0.0066; -0.0003]**
TV → screen → BMI	n.a.	**0.0587 [0.0016; 0.1877[3]]**	**0.0177 [0.0014; 0.0475[3]]**
TV → screen → sleep → BMI	n.a.	**0.0115 [0.0016; 0.0368[3]]**	**0.0026 [0.0004; 0.0078[3]]**
TV→ sleep → BMI	n.a.	-0.0298 [-0.1044; 0.0045[3]]	**0.0170 [0.0013; 0.0467[3]]**
Screen → sleep → BMI	**0.0004 [0.0001; 0.0010[3]]**	n.a.	n.a.

OLS regression-based path analysis was used to estimate direct and indirect effects (unstandardized B), all models were adjusted for gender. Bold printed coefficients were significant pathways.

CI: confidence interval; Screen: screen time (minutes/day); sleep: sleep duration (minutes/day); n.a.: not applicable; TV: television

[1] TV= TV in bedroom (0: no, 1: yes)

[2] TV= Number of TVs at home (1: ≤2 TVs, 2: 2 TVs, 3: >2 TVs)

[3] Bias corrected bootstrap 95% CI

Model 1: Screen time, sleep duration, BMI; Model 2a: Model 1 + TV in bedroom; Model 2b: Model 1 + Number of TVs at home

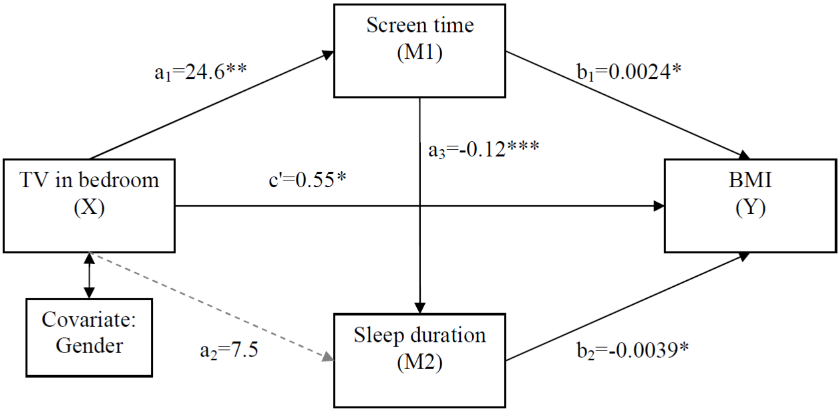

Figure 2. Model 2a: a serial multiple mediator model with television (TV) in the child's bedroom (no=0, yes=1), screen time (minutes/day), sleep duration (minutes/day) and BMI. Path coefficients (unstandardized B) of the components of the indirect effects (a and b) and the direct, independent effect (c')

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

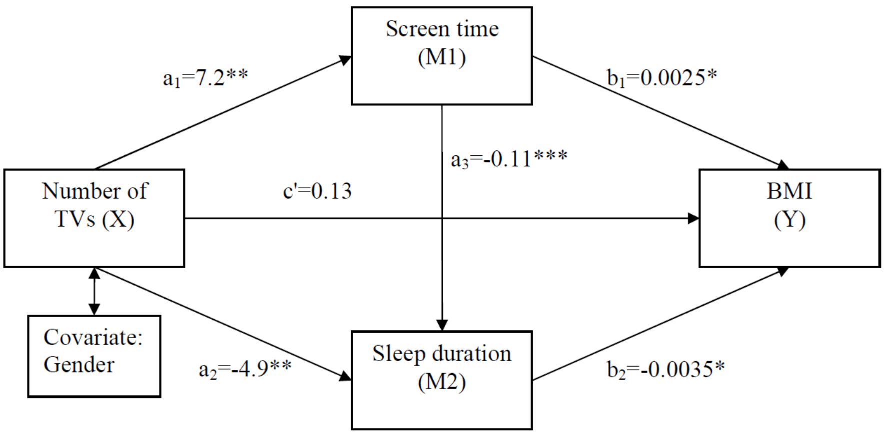

Figure 3. Model 2b: a serial multiple mediator model with number of televisions (TVs), screen time (minutes/day), sleep duration (minutes/day) and BMI. Path coefficients (unstandardized B) of the components of the indirect effects (a and b) and the direct, independent effect (c')

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

DISCUSSION

Sleep duration, screen time and a television in the bedroom as well as the number of televisions at home are related to each other and are independently related to BMI, except for the number of televisions at home. Outdoor play is inversely associated with screen time, but not with BMI or sleep duration. Thus, the assumption that watching television is related to less outdoor play is correct, but our findings do not support that this is related to a higher BMI in preschool children. The effect of watching television on BMI is rather acting trough less sleep, than less outdoor play.

In addition to the existing studies investigating one or two aspects of the associations between sleep duration, television time and outdoor play with overweight in children younger than 5 years of age, we focused on the interrelation between those factors. Moreover, we included the number of televisions or having a television in the bedroom in the model. Previous literature, regarding the relation between watching television, or a television in the bedroom, and BMI in children younger than 5 years, confirms our results. Watching television in children this young was associated with overweight (16,26-28). It was also found that a television in the bedroom was associated with a higher BMI and with more time watching television (28). A television in the bedroom was found to increase television viewing (29,30) and parents underestimated the amount of time watching television when the children had a television in their bedroom (29). Therefore, when parental reports of television time are used, it is necessary to take into account whether or not the child has a television in the bedroom. We found that children who had a television in the bedroom had a higher BMI independent of the amount of time they watched television according to their parents. So possibly, these parents indeed underreported screen time and/or overestimated sleep duration.

Excess time in watching television may limit the time a child sleeps (16-18,31). Sleep duration in children aged younger than 5 years old, is inversely association with overweight (32,33) and subsequently with childhood overweight (18,26,34-37). In one study no association between sleep duration at age younger than 5 years and overweight or subsequent childhood overweight was found (38). In adults, sleep deprivation can cause a change in appetite regulating hormone levels, resulting in increased hunger and appetite (39-42). In children, little is known about the underlying mechanism, but it was found that shorter sleep duration was associated with higher consumption of energy-rich foods (43). Secondly, in adults, shorter sleep duration is also associated with fatigue and reduced physical activity, resulting in less total energy expenditure in adults (44,45). In children aged 3-5 years a positive relation was found between physical activity and sleep duration (46). Finally shorter sleep duration gives more opportunity to eat, especially in the evening after dinner (11,47,48). A study in 5-6 year old children found that eating snacks while watching television was associated with a lower sleep duration, which gives a higher chance of being overweight (49). We expect that decreased sleep duration increases the risk for a higher BMI. An alternative explanation is that obesity can cause sleep problems, like obstructive sleep apnoea (50,51). Since sleep problems were related to more severe forms of overweight like obesity (52) rather than to overweight and only 2% of the children in this study were obese, we do not expect that the results in our study are explained by sleep problems.

The assumed association we found between watching more television and less outdoor play has not been confirmed (19-21). Playing outside could be protective for the development of overweight due to increased energy expenditure. In children aged 5 and 10-17 years it was found that less playing outdoor games was associated with overweight (22,53). In contrast, in 3 other studies outdoor play was not associated to overweight in children aged 3-12 years old (19,23,54). In our study we neither found an association between outdoor play and BMI. A possible explanation is that in young children a lot of activities outdoor are not specifically different from activities indoor.

An assumption not investigated in our study is the association of eating habits with sleep duration and watching television. Eating habits can mediate the relation of sleep duration and watching television with BMI. In two previous studies from a Dutch cohort the number of sugared drinks and snacks did not affect the positive association between television viewing and BMI (55) or the negative association between sleep duration and BMI in 4-8 year old children (56). The supposed effects of sleep on hunger and satiety may translate in increased energy intake in several ways, either through food preferences, portion sizes or desire for snacking more. To adequately assess this in children of 3 and 4 years of age is a challenge for future research.

To conclude, short sleep duration, long screen time and a television in the bedroom may contribute direct and indirectly to the development of overweight in children aged 3 and 4 years. The assumption that watching television is related to less outdoor play is correct, but our findings do not support that this is related to a higher BMI in preschool children. These results can be implemented in prevention programs for overweight in young children.

ACKNOWLEDGEMENTS

The study was sponsored with an unrestricted grant by Hutchison Whampoa Limited, 22/F Hutchison House, 10 Harcourt Road, Hong Kong. The study sponsor had no role in 1) the design and conduct of the study; 2) the collection, management, analysis, and interpretation of the data; 3) the preparation, review, or approval of the manuscript; and 4) the decision to submit the manuscript for publication.

CONFLICTS OF INTEREST

No conflict of interest was declared.

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Chapter 8

Parental determinants of physical activity and body composition in young children-GECKO Drenthe

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Submitted

ABSTRACT

PURPOSE. Parental behavior can influence the development of their children's overweight at different stages of their child's development. The aim of this study is to examine whether parental BMI and physical activity are associated with BMI, waist circumference and physical activity in children.
METHODS. In 3-4 year old children, weight, height and waist circumference were measured. Physical activity was measured in a subgroup (n=299) using a tri-axial activity monitor. Parental weight and height were self-reported and parental physical activity was assessed by a validated questionnaire.
RESULTS. In total 1554 children (age 3.9±0.1 years, BMI 15.8±1.3 kg/m2 and waist circumference 52.4±3.5 cm) were included. Eleven percent was overweight or obese. Maternal BMI was negatively correlated to daily physical activity of children (r=-0.158, p=0.007). As expected, parental BMI was positively associated with children's BMI and waist circumference (r=0.20-0.27, p<0.001). Maternal physical activity used for active commuting, either walking or biking to work or school, showed a negative correlation with BMI of the child (ϱ=-0.062, p=0.042). No correlation between total physical activity of the parents with the child's BMI, waist circumference or physical activity was found.
CONCLUSION. Higher maternal BMI was related to less children's physical activity, whereas more active commuting by the mother and a lower parental BMI were related to a lower BMI of the children. A healthier lifestyle of the parents may contribute to a healthier BMI of both preschool children and their parents.

INTRODUCTION

Obesity in childhood will contribute to obesity-related adverse health at adult age, because children with overweight or obesity have a high chance to be obese in adulthood (1). Once overweight, it is hard to achieve a normal weight. Furthermore, intervention studies show that intervention at early age give the highest chance of success to both prevent and treat overweight or obesity in later life (2-4).

Physical activity can prevent overweight, because it increases the energy expenditure. Investing in physical activity during early years might have health benefits later in life, particularly with respect to body composition (5). Children's habitual physical activity is associated with a lower percentage body fat in preschool children (6) and can protect children from developing overweight (7). Besides prevention of overweight, physical activity has many other health benefits. Various reviews support a positive relationship between increased physical activity and better psychosocial health, cognitive development, aspects of cardiometabolic health, like lipid profiles and insulin resistance, skeletal health and motor skill development (5,8,9). Furthermore, the development of motor skills is a key factor in the likelihood of participation in various forms of physical activity later in life (10). Finally there is evidence that obesity (1,11), inactivity patterns (12) and physical activity levels (13) may all track from childhood to adolescence and adulthood.

Parents can influence the development of their children's overweight at different stages of their child's development. At the same time, the best strategy for recognition and treatment of overweight at young age is not clear yet. Already during gestation, maternal factors, like high pre-pregnancy BMI and weight gain during pregnancy, can increase the risk for obesity in the offspring (14). Some studies found a relation between physical activity during pregnancy and body fat at age 5 (15). During infancy and early childhood parents play an important role in the development of habits related to eating and physical activity. At that young age, parents can shape a healthy environment to encourage the development of a healthy diet and daily habitual physical activity patterns (16). Parental physical activity and support can encourage children to be active in their daily habits, by being a role model for their children, or by actively participating in physical activity together with their children.

Firstly, obesity and physical activity track from childhood to adulthood; so that once overweight, it is hard to achieve normal weight. Secondly, increased physical activity is related to better motor skill development, what is associated with physical activity later in life. So, research has to focus on the preschool years (<5 years). Studies investigating the effect of parental physical activity on the physical activity level of preschool children are limited.

Therefore, the aim of our study is to examine whether parental BMI and parental physical activity are associated with BMI, waist circumference and physical activity in 3 and 4 year old children.

METHOD

Subjects

The GECKO Drenthe birth cohort is a population based birth cohort studying early risk factors for overweight and obesity in young children. Children are born between 2006 and 2008 in Drenthe, a northern province of the Netherlands. Details of the study design, recruitment and study procedures were described in detail elsewhere (17). At baseline, in 2006-2008, parents of 2997 children intended to participate in the study, of whom 2874 actively participated. Missing data are mainly due to logistic and organizational problems. For all children, written informed consent was obtained from parents, and the study was approved by the Medical Ethics Committee of the University Medical Center Groningen (UMCG) and follows the declaration of Helsinki.

Anthropometric measurements

At the age of 24, 36, 45 and 60 months, children were measured by trained nurses according to a standardized protocol. Weight was measured in light clothing using an electronic scale with digital reading, and recorded to the nearest 0.1 kg. Height was assessed using a stadiometer and recorded to the nearest 0.1 cm. Waist circumference was measured twice using a measure tape midway between the lowest rib and the top of the iliac crest at gentle expiration over the naked skin in standing position to the nearest 0.1 cm. BMI was calculated as weight (kg) divided by squared height (m). BMI for age Z-scores and waist circumference for age Z-scores were calculated according to the reference tables of the Netherlands 1997 using Growth Analyser 3.5 © (Dutch Growth Foundation, Rotterdam, the Netherlands, http://www.growthanalyser.org). To calculate the correlation of parental physical activity and BMI with children's BMI or waist circumference, data obtained at child's age 45 months were used. To calculate the relation between children's physical activity (measured between the age of 2.7 and 5.1 years old) and their BMI or waist circumference, the available BMI Z-score and waist circumference Z-score closest to the measurement were used.

Parental BMI was assessed from self reported weight in kg (before pregnancy) and height in cm in a questionnaire about parental characteristics before birth of the children. At the children's age of 18 months parental weight was again reported in a questionnaire. Height from the first questionnaire and weight from the second questionnaire were used to calculate BMI. If weight from the second questionnaire was missing, weight from the first questionnaire was used. In 54% of the mothers and 53% of the fathers, BMI was based on the second questionnaire. BMI values from those parents who had had BMI in both the first and the second questionnaire were highly correlated ($r = 0.89$-0.92, $p < 0.001$).

Physical activity

Children's physical activity was assessed by the DirectLife tri axial accelerometer for movement registration, TracmorD (Philips DirectLife, Amsterdam, the Netherlands). The accelerometer was worn when the children were awake, except for water activities, in a small case on a belt on the middle of the lower back. TracmorD provides moderate-to-strong validity evidence that supports its use to evaluate physical activity level and energy used for activity in 3 and 4 year old children (18). Output of the accelerometer is defined as mean activity counts per minute (ACM). ACM is calculated as the sum of all counts/min during the wear period divided by the total amount of wear time in minutes. The measurement of physical activity was valid when the accelerometer was worn at least 400 minutes/day for a minimum of 3 days, including at least 1 weekend day and 2 week days. No categories were made in amount of time in moderate and vigorous physical activity, because reliable and validated cut-off points in children in this age category for the various intensities of physical activity are not yet available.

At child's age of 45 months, parental physical activity was assessed by the validated questionnaire SQUASH (Short QUestionnaire to ASsess Health enhancing physical activity) (19). The SQUASH estimates habitual physical activities and is prestructured in commuting activities, leisure time activities, sports, household activities, and activities at work or school. Questions included type of activity, duration, frequency and intensity. Total amount of physical activity in minutes per week was calculated and outcomes were analyzed as time spent in light physical activity, moderate physical activity and vigorous physical activity, as well as physical activity in categories of commuting, leisure time, sports, household, and activities at work or school, according to Wendel-Vos et al. (19). Parents who spend more than 7560 min/week (more than 18 h/day) on physical activity were excluded, because of their impossible high time in physical activity.

Statistics

Data are presented as means with SD and medians with the 25th to 75th percentiles. Pearson correlations coefficients were used to analyze the relationship of parental BMI with children's BMI Z-scores, with children's waist circumference Z-scores and with children's physical activity. The relationship of children's physical activity with their own BMI Z-scores, and their waist circumference Z-scores was also analyzed using Pearson correlations coefficients. Spearman correlations coefficients were used to analyze the relationship of parental physical activity with children's BMI Z-scores, with children's waist circumference Z-scores and with children's physical activity. The relationship between parent's physical activity and their own BMI was also analyzed using Spearman correlations coefficients. Statistical analyses were performed using SPSS 20.0.0.1 for Windows (SPSS, Chicago Illinois, USA). The significance level was set to $p < 0.05$ (2-tailed).

Table 1. Clinical characteristics of the children

	At age 45 months		**At age closest to PA measurement**	
	N	**Mean ± SD or N (%)**	**N**	**Mean ± SD or N (%)**
Boys	780 (50%)	-	157 (53%)	-
Age (yrs)	1554	3.9 ± 0.1	298	3.6 ± 0.6
BMI (kg/m^2)	1554	15.8 ± 1.3	298	15.9 ± 1.3
BMI Z-score[1]	1554	0.11 ± 0.92	298	0.09 ± 0.89
Waist (cm)	1164	52.4 ± 3.5	242	51.5 ± 3.6
Waist Z-score[1]	1164	0.39 ± 0.91	242	0.28 ± 0.93
OW/obese[2]	1554	167 (11%)	298	30 (10%)
Total PA (ACM)[3]	-	-	299	3715 ± 712

ACM: counts per minute; OW: overweight; PA: physical activity.

[1] According to reference tables of the Netherlands, 1997.

[2] overweight and obesity defined according to Cole 2000 (20).

[3] average counts per minute for wake hours.

RESULTS

Characteristics of the children are shown in table 1. In total, 1554 children, with an age of 3.9 ± 0.1 years, BMI 15.8 ± 1.3 kg/m², and waist circumference 52.4 ± 3.5 cm, were included together with the parents. Eleven percent of the children were either overweight (8.4%) or obese (2.3%). Clinical characteristics of the parents are shown in table 2. The activity pattern was measured in 299 children, and there was no significant difference in either weight, BMI or waist circumference between the total group and the group in whom activity was measured.

Table 2. Clinical characteristics of the parents

	N	Mean ± SD or N (%)	Median [25th-75th percentile]
Father characteristics			
Age at birth child (yrs)	2605	33.9 ± 4.9	33.9 [30.6 - 36.9]
BMI (kg/m²)	2516	25.4 ± 3.3	25.0 [23.2 - 27.2]
Overweight[1]	2516	1028 (41%)	-
Obese[2]	2516	222 (9%)	-
Total PA (min/week)	1236	3451 ± 1117	3390 [2872 - 4020]
LPA (min/week)	1236	2285 ± 1260	2575 [1140 – 3180]
MPA (min/week)	1236	1033 ± 1160	420 [140 - 1950]
VPA (min/week)	1236	134 ± 234	30 [0 - 180]
Mother characteristics			
Age at birth child (yr)		31.3 ± 4.4	31.3 [28.3 – 34.4]
BMI (kg/m²)	2613	24.7 ± 4.6	23.7 [21.5 - 26.7]
Overweight[1]	2613	656 (25%)	-
Obese[2]	2613	312 (12%)	-
Total PA (min/week)	1303	3468 ± 1353	3270 [2570 - 4224]
LPA (min/week)	1303	2705 ± 1295	2580 [1815 – 3480]
MPA (min/week)	1303	698 ± 688	450 [225 - 960]
VPA (min/week)	1303	65 ± 121	0 [0 - 90]

LPA: light physical activity; MPA: moderate physical activity; PA: physical activity; VPA: vigorous physical activity.

[1] BMI = 25.0-29.99; [2] BMI ≥ 30

Table 3. Correlations of parental and child factors with physical activity and body composition in 3 and 4 year old children

	Child								
	Total PA (ACM)			BMI Z-score			Waist circumference Z-score		
	Correlation coefficient	p-value	n	Correlation coefficient	p-value	n	Correlation coefficient	p-value	n
Mother									
Commuting PA (min/wk)[1,2]	0.003	0.992	230	**-0.062**	**0.042**	**1079**	-0.013	0.729	735
Total PA (min/wk)[2]	0.097	0.144	230	0.016	0.589	1079	0.025	0.499	735
LPA (min/wk)[2]	0.096	0.148	230	-0.021	0.492	1079	-0.016	0.667	735
MPA (min/wk)[2]	-0.034	0.609	230	0.056	0.065	1079	0.060	0.103	735
VPA (min/wk)[2]	0.064	0.333	230	-0.021	0.500	1079	-0.032	0.381	735
BMI (kg/m^2)[3]	**-0.158**	**0.007**	**291**	**0.270**	**<0.001**	**1448**	**0.215**	**<0.001**	**1088**
Father									
Commuting PA (min/wk)[1,2]	0.016	0.813	227	0.030	0.346	1023	0.007	0.861	688
Total PA (min/wk)[2]	0.044	0.507	227	0.039	0.216	1023	0.026	0.499	688
LPA (min/wk)[2]	0.011	0.871	227	0.006	0.859	1023	0.044	0.252	688
MPA (min/wk)[2]	-0.014	0.832	227	0.031	0.324	1023	-0.001	0.975	688
VPA (min/wk)[2]	0.041	0.543	227	0.015	0.636	1023	0.015	0.692	688
BMI (kg/m^2)[3]	-0.067	0.256	291	**0.237**	**<0.001**	**1405**	**0.203**	**<0.001**	**1060**
Child									
Total PA (ACM)[3]	-	-	-	**0.147**	**0.042**	**193**	0.143	0.072	159

ACM: activity counts per minute; LPA: light physical activity; MPA: moderate physical activity; activity; PA: physical activity; VPA: vigorous physical activity.

[1] by bike or walking; [2] Spearman correlation coefficient; [3] Pearson correlation coefficient

Correlations of parental and child factors with physical activity, BMI and waist circumference in the children are shown in Table 3. BMI of both mother and father strongly correlated with the BMI Z-score and the waist circumference Z-score of the children, all $p < 0.001$. Maternal BMI showed a negative correlation with the activity pattern in all children ($r = -0.158$, $p = 0.007$), and after posthoc analysis for gender this was stronger in girls ($r = -0.167$, $p = 0.04$) than in boys ($r = -0.133$, $p = 0.123$). No correlation between the BMI of the father and activity pattern of the child was found.

In both father and mother, no correlation between their total activity pattern and the activity pattern of the children was found. In mothers, commuting to school or work either by walking or biking showed a negative correlation with the child's BMI ($r = -0.062$, $p = 0.042$). The total, light, moderate or vigorous physical activity of the mother showed no correlation with the BMI of the children. The total, light, moderate or vigorous activity level of the father also showed no correlation with the BMI Z-score of the children. In mothers, less sports activity, ($\varrho = -0.085$, $p = 0.003$), less leisure time activity ($\varrho = -0.083$, $p = 0.003$), and less vigorous physical activity ($\varrho = -0.084$, $p = 0.003$) were related to a higher BMI of the mother. In the fathers, more leisure time activity ($\varrho = 0.075$, $p = 0.011$) and less household activity ($\varrho = -0.108$, $p < 0.001$) were related to a higher BMI of the father. Physical activity, in both mother and father, was not associated with children's waist circumference Z-score.

Finally, in children a positive relation between physical activity and BMI Z-score was found, so that more physical activity indicated a higher BMI ($r = 0.147$, $p = 0.042$). No significant association between physical activity and waist circumference Z-score was found.

DISCUSSION

BMI of the mother influences the activity level, the BMI and the waist circumference of the child, while a higher BMI of the father is related to a higher BMI and waist circumference of the children. More active parents do not have more active children, but we found an inverse relationship between active commuting of the mother with children's BMI.

Genetic predisposition, but maybe more important, the obesogenic environment may be underlying factors to explain these findings. In young children, parents have a strong influence on their children's lifestyle. They play an important role in the development of habits related to eating and physical activity (16). Parents with overweight may create an obesogenic environment for their child, which results in a higher risk of overweight in these children. Active commuting in adults may have an important role in changes in their BMI over time (21). We found a correlation between higher maternal active commuting time and a lower children's BMI. When a mother goes to her work by bike or walking, she will bring her child walking or biking with her to go to the school or daycare. We found no relation between active commuting and total physical activity of the child. So, the effect was not seen directly on physical activity, but these results might indicate that when mothers actively participate with their children in daily physical activity it will contribute to a healthier BMI of their children.

The parental BMI might be an indicator of an obesogenic environment for the child. Indeed, a higher parental BMI is not only associated to a higher BMI of the child, but a higher maternal BMI was also related to less physical activity of the child. Mothers with a higher BMI may create a more obesogenic environment which may include less physical activity with the child, or less stimulation of physical activity in the child. This might also be related to our finding that mothers with a higher BMI were less active themselves. Our data are in line with a review (22) that showed that both maternal and paternal BMI are related to a higher BMI Z-score and waist circumference Z-score in the children.

In our study, the relation between parental behavior and obesity in children is mainly attributed to mothers, but not to fathers. In the Netherlands it is common that both mother and father have a job and combine the care for their child, but still mothers spent the most time in raising their child. Women have more often part time jobs compared to men (23), and children of divorced parents live more often with their mother, than with their father (24). We hypothesize that the influence of an obesogenic environment on the child is stronger determined by the mother than by the father.

Some previous studies investigated the relation between parental physical activity and/or BMI with their preschool children's physical activity, but only limited studies measured physical activity with accurate methods, like accelerometry or validated questionnaires (25-27). Three studies found a positive relationship between parental physical activity and their preschool children's PA. In these studies, children's physical activity was measured with an accelerometer (25-27) and parental physical activity was measured with an accelerometer (25,26) or a validated questionnaire (27). These studies measured physical activity in children for a longer period than that we did in our study, i.e. 5-9 days instead of 4 days. Two studies measured parental physical activity by accelerometer; it might be that this would give better results than measurement of physical activity by a questionnaire, like we did. On the other hand, the questionnaire provides more information on type of activity and on structured activities like active commuting. One study found no direct relation between parental and child physical activity, but the previous reported associations may have been indirect, showing that parental physical activity was positively associated with parental physical activity support, which in turn was positively associated with their children's physical activity (28). Parental BMI predicting preschool children's PA, was found in one study for BMI of the father, but not of the mother (29), while another study did not find this relation (26). We found this relation only in mothers, but not in fathers. More research is needed to draw firm conclusions about this relation in preschool children.

Another aspect of a child's living environment is parental modeling. We found no relation between total, light, moderate or vigorous parental physical activity and children's physical activity or BMI. Possibly at this young age parental physical activity does not trigger young children to be physical active. At this young age, parents may not be a role model for children's physical activity behavior yet. Young children may not be intrinsically aware of their parents being active at the gym, or being out for a jog. The exception may be the previously discussed active commuting time of the mother, which can be expected as an activity in which the child is involved. As highlighted before, at a young age it seems that parents participating in physical activity with their children is a more important factor than the total amount of physical activity of the parents.

We found no studies investigating the relation between parental physical activity and preschool children's BMI. Studies in older children (7-12 years) and adolescents (11-18 years) did not show consistent results. One study in older children (10-12 years of age) found that in mothers physical activity was positively related overweight in their children (30). Two studies with children aged 7-12 years found no association between physical activity of the parents and children's overweight or obesity (31,32). One study in adolescence (11-18 years of age) found an inverse relation between parental physical activity and adolescents' overweight (33). Compared to our study, the children in these studies were older and only total physical activity of the parents was measured.

Therefore, more research is needed, especially in preschool children, regarding the influence of parental physical activity on children's BMI.

Some findings were not in line with our hypothesis that a higher level of physical activity relates to a lower BMI, because we found that more active children had higher BMI. Surprisingly, this is also found in previous studies in preschool children: Pate et al. also found a positive relation between BMI and physical activity in 3 to 5 year old children (34); and Jackson et al. found this relation in children aged 2 to 6 years (35). However, most other studies in preschool children found no relation between physical activity and BMI (29,36-41). These results can be caused by the uncertain reliability of BMI as indicator of increased fat mass in this age group. BMI is not only dependent on fat mass but also on muscle mass (42,43). It is possible that misclassification for mild overweight obscured the relation between BMI and physical activity. In a review we found that not BMI, but body fat percentage is related to physical activity in preschool children (6)). Unfortunately, we did not measure fat mass in these children. As a proxy for fat mass, we used waist circumference, for financial and logistical reasons. In this study we did not find differences in results when we used either BMI or waist circumference. It is unlikely therefore that we would have found different results when we would have measured fat mass. Thus, it seems that the relation between physical activity and BMI or body fat can be dependent on age. A review of Jimenez-Pavon et al. (44) found that the relation between physical activity and adiposity was found more often with increasing age. The inverse relation was found in 60% (n = 3) of preschool studies; 77% (n = 17) of studies of primary school-age children, and 86% (n = 18) of studies of adolescents (44).

A strength of our study is the measurement of physical activity of both parents and children with validated methods and in children with an objective method, the accelerometer. The drawback is that measurements were only performed in a subgroup. Still, we obtained data in almost 300 children. Furthermore, there were no differences in clinical characteristics between the children in whom the activity pattern was measured and the total group of children. Therefore, potential bias due to selection of children is less likely. A second drawback is that due to lack of validated cut-offs, we could not categorize children's total physical activity into light, moderate and vigorous physical activity.

To conclude, BMI of both parents is related to the BMI and waist circumference of their children. Higher maternal BMI was related to less children's physical activity, whereas more active commuting by the mother was related to a lower BMI of the children. We hypothesize that interventions designed to treat or prevent obesity in children should not only focus on the child, but also on the obesogenic environment. Parental behaviors directly influencing the children, like actively participating in physical activity with their children, eating healthy food together with their children and forward their healthy food patterns, are more important than focusing only on the health of parents themselves. A healthier lifestyle of the parents may contribute to a healthier BMI of both preschool children and their parents.

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Chapter 9

General discussion

The present thesis focused on physical activity and overweight in young children. From available studies we know that intervening in children with obesity at an early age can be effective (1,2) and that intervention at young age may be more effective than intervention later in life (2). Furthermore, obesity (3,4) and physical activity (5) track from childhood to adulthood; once overweight is established, it is hard to achieve normal weight. Increased physical activity is related to improved health later in life (6) and to better motor skill development, which is associated with physical activity later in life (7). Therefore, research to prevent obesity and overweight has to focus on the preschool years (<5 years).

The first objective of this thesis, described in Part I, was to validate and evaluate methods used to assess overweight, energy used for maintenance and growth, and energy used for physical activity in preschool children. The second objective, described in Part II, was to examine correlates of physical activity, sedentary behavior and overweight in preschool children. This chapter provides a short summary of: the characteristics of the GECKO Drenthe cohort; methodological issues in the measurement of physical activity, energy expenditure and overweight in preschool children; a discussion of the correlates of activity behavior and overweight in preschool children; the clinical implications; and directions for future research.

GECKO DRENTHE COHORT

Most studies in this thesis are performed within the GECKO Drenthe birth-cohort. GECKO Drenthe is a birth-cohort within the Groningen Expert Center for Kids with Obesity (GECKO) and was designed to assess risk factors for childhood obesity. Detailed information about the cohort is described in the introduction. The cohort included 2997 children of whom 2874 ever actively participated. Most studies in this thesis were based on measurements at age 3 and 4 years. In the 3 and 4 year old children (mean age 3.9 ± 0.1 years) weight was 17.6 ± 2.3 kg; their height was 105.4 ± 4.1 cm; their BMI was 15.8 ± 1.3 kg/m^2; and their waist circumference was 52.4 ± 3.5 cm. Eleven percent were overweight (8.4%) or obese (2.3%). A recent survey in the Netherlands showed that, in children aged 3 and 4 years, 7-14% have overweight and 1-3% are obese (8). In 2003, in the province Drenthe it is found that of 5 year old children 10% had overweight and 3% were obese. We found in our cohort in 2012-2013 that at the age of 5 years, 13% had overweight and 3% were obese. A slightly higher prevalence of overweight can be explained by the increase in the prevalence of overweight and obesity over time. We conclude that our cohort is representative for the Netherlands and for Drenthe according to overweight and obesity rates.

PART I. METHODOLOGICAL ISSUES IN THE MEASUREMENT OF PHYSICAL ACTIVITY, ENERGY EXPENDITURE AND OVERWEIGHT IN PRESCHOOL CHILDREN

To assess risk factors for the development of overweight, valid and reliable instruments are needed to measure or estimate the determinants and the outcome as accurate as possible.

Methods to assess overweight

Overweight is defined as excess body fat. The four-component-model is used as a reference method to define body fat. This model divides the body into fat mass, fat-free water, fat-free protein, and fat-free mineral. Underwater weighting, air-displacement plethysmography, dual energy X-ray absorptiometry (DXA) and total body water, determined by D_2O dilution, are almost as good as the four component-model (r>0.9) (9). Therefore, these measurements are the most accurate measures to determine the amount of body fat and to define overweight. Skinfold thicknesses and bio electrical impedance analysis (BIA) also provide information on body fatness. However, the accuracy of skinfold thickness depends highly on the skills of the examiner, it is imprecise with large inter-observer variability and measurements are often biased. Body fat measured by BIA has low correlations with body fat measured by more accurate methods (9). Because measurements of body fat are time consuming and expensive, proxy measures, like BMI, waist circumference, waist-to-height ratio or waist-to-hip ratio, are used to define overweight.

In **Chapter 2** we performed a review of available studies investigating the association between physical activity and adiposity in preschool children. Only a limited number of studies used percentage body fat as outcome for adiposity, most studies used a proxy measure for adiposity, like BMI. The review showed that in children aged 1.5 to 6 years old an inverse relation exists between physical activity and body fat percentage, while the relation was not found with BMI. Therefore, the relation is dependent on which measure of overweight in children is used.

In **chapter 3**, we examined whether waist-to-height ratio is a better measure than waist circumference and BMI, as indicator of body fat percentage and cardiometabolic risk factors in children aged 3-7 years.

BMI is a commonly used measure to define overweight and obesity, however its reliability is uncertain for this age group in particular because BMI is not only dependent on fat mass but also on muscle mass. In relatively fat children, BMI is a good indicator of excess body fat. However, in children classified as overweight, a high BMI is more often explained by relatively large muscle mass (10,11) leading to frequent misclassification. Overlap in percentage body fat values is apparent between children with normal weight, overweight, and obesity based on BMI (12). One study found that 30% of the children with a BMI-for-age between the 85th and 94th percentiles (overweight) had a body-fatness level that was comparable to that among normal-weight children (13). The accuracy of BMI increases with increasing levels of body fat, but differences in the BMI of relatively thin children can be largely due to fat-free mass (10). BMI can be used when those classified as obese are compared to those classified as normal weight. Unfortunately, this is not feasible in our studies because only a small number of children have obesity.

In adults it is found that waist-to-height ratio is a better and more feasible measure to assess overweight than BMI and also cardiometabolic risk factors, especially among people with different ethnicities and different types of body composition (android shape vs. gynoid shape) (14,15). Waist-to-height ratio provides information about body fat distribution. Central fat distribution is associated with greater health risks than total body fat (16,17). In adults a general cut-off value of 0.5 for overweight can be used for both men and women across many ethnicities (14,15). One cut-off value of waist-to-height ratio for all ages during childhood and adolescence is not feasible, because waist-to-height ratio decreases over age (18,19). Specific age related cut-off values are needed because humans get a smaller waist compared to their length when they grow up. It was found that the most sensitive waist-to-height ratio cut-off to identify children having ≥85th percentile for body fat percentage was ≥0.46 for male subjects and ≥0.45 for female subjects aged 8–16 years (20). The advantage of waist-to-height ratio over waist circumference is that waist-to-height ratio adjusts for height. When compared to short people with the same waist circumference, tall people have lower levels of cardiometabolic risk factors and a 30% lower prevalence of the metabolic syndrome (21). In a recent published letter in the ‘Economist’ it is also argued that with the current BMI formula, in short people BMI is underestimated and in tall people it is overestimated (http://people.maths.ox.ac.uk/trefethen/bmi.html). Another proxy measure of body fat is waist-to-hip ratio. In Chinese adults it is found that waist-to-hip ratio is the best adiposity measure to predict type 2 Diabetes Mellitus (22). In children, these strong associations with cardiometabolic risk factors are not expected, because differences in body composition, the more central type of fat distribution (android shape) vs. whole body peripherally fat distribution (gynoid shape), are not expressed yet. In agreement with this statement, we found a high correlation between waist and hip circumference in the children from a normal population, included in **chapter 3** ($r = 0.84$, $p < 0.001$). Also both waist circumference ($r = 0.48$-0.56) and hip circumference ($r = 0.61$-0.78) were associated with body fat percentage. This supports our idea that body fat at in children is spread more equally over the body.

In **chapter 3** we found that in children of 3 and 4 years, not waist-to-height ratio, but waist circumference was best associated with body fat percentage, measured by isotope dilution method in the crude model. After correction for age and gender, all 3 proxy measures: waist-to-height ratio; waist circumference and BMI, were almost equally associated with body fat percentage. In children aged 6-7 years, BMI showed the highest association with body fat percentage, measured by isotope dilution method, both in the crude model and after correction for age and gender. In overweight children aged 3-5 years, BMI and waist circumference were almost equally associated with body fat percentage, measured by BIA, both in the crude model and after correction for age and gender. Next to the relation with body fat percentage, we also examined the relation of waist-to-height ratio, waist circumference and BMI with cardiometabolic risk factors in the obese children (3 to 5 years). Waist-to-height ratio, waist circumference and BMI were positively correlated with systolic blood pressure, HOMA2-IR, leptin and triglycerides. For adiponectin we found only a significant inverse correlation with waist circumference and for HDL-cholesterol only an inverse correlation with waist-to-height ratio. We found that, except HDL-cholesterol, none of the cardiovascular risk factors were better correlated with waist-to-height ratio than with BMI or waist circumference. From experience in the GECKO Drenthe cohort, nurses from the health municipalities pointed out that waist measurement is not easy; children blow up their belly or keep their breath, which makes the measurement of waist circumference less accurate. Moreover, children don’t mind being measured, but weight measurement is much easier and more pleasant that the measurement of waist circumference. Because weight measurement, used to calculate BMI, is a more accurate and more pleasant measure than waist circumference, we conclude that BMI in young children is the most feasible proxy measure of adiposity, although measurement of body fat, e.g. by DEXA, would distinguish better between children with high and low body fat percentage.

We found that BMI was better correlated to body fat percentage and cardiometabolic risk factors than waist-to-height ratio, while in children from the age of 8 and adults the opposite was found (14,20). This finding can be attributed to the change in body composition over age. In adults, people with high visceral fat are seen, while in young children fat is more gradually spread over the body. Visceral fat, which is associated with higher health risks than subcutaneous fat, accumulates with age (23,24). We conclude that the results from waist-to-height ratio, waist circumference or BMI did not give large differences in their relation with body fat percentage and cardiovascular risk factors in young children.

Methods to assess energy expenditure

Total energy expenditure is the sum of energy needed for maintenance, activity, growth and diet-induced thermo-genesis.

The energy needed for maintenance and growth, or the basal metabolic rate, can be measured by either direct or indirect calorimetry, but more often it is estimated according to different equations. In **chapter 4** we compared energy metabolism measured by indirect calorimetry under standardized conditions against existing equations including Schofield, the FAO/WHO/UNU, Oxford and Harris-Benedict in 3 and 4 year old children. We measured the metabolic rate during sleep as measure for the energy needed for maintenance. We found lower values of energy used for maintenance than can be calculated from existing equations.

Measuring basal metabolic rate (defined as energy expenditure in resting but awake state, supine, thermo-neutral, during fasting) in infants and young children is not feasible, since the child should be fasted for 12 hours and – more problematic- the child must stay awake but quiet during at least 30 minutes while situated under a ventilated hood system. Therefore, in young children the sleeping metabolic rate is used as a measurement as close to the basal metabolic rate as possible. The energy for growth, or diet induced thermo-genesis in adults, is included in the metabolic rate when that is measured in the non-fasting state, soon after a meal. The energy used for diet induced thermo-genesis, as it is already shown by Brooke and Asworth in 1972, is in fast growing children related to the rate of growth (25). The energy requirements for diet induced thermo-genesis therefore, includes the energy needed for growth. This also indicates that growth takes place especially after a meal (25-28). Sleeping metabolic rate, when measured soon after a feeding, as done by us, will be higher than the basal metabolic rate due to the energy used for growth. In considering all this, one must realize that the contribution of the dietary induced thermo-genesis or energy used for growth is rather small in young children. Studies have shown that the energy required for tissue synthesis is around 2 kcal/gram growth. The growth of a 3 or 4 year old child is around 6 gram/day (29). The energy used for growth by these children therefore only is 12 kcal/day, which implies a minimal effect on the energy balance.

The energy for maintenance is considered to be equal to the basal metabolic rate. The question rises if the sleeping metabolic rate is an adequate measure to express the energy used for maintenance in young children. A study of Wouters-Adriaens & Westerterp found that in 10 year old children the overnight sleeping metabolic rate was lower than the basal metabolic rate, measured in the morning, under standardized conditions. In contrast, in adults they found that overnight sleeping metabolic rate and (morning) basal metabolic rate were equal, while in elderly the overnight sleeping metabolic rate was higher, than the (morning) basal metabolic rate. We believe that the sleeping metabolic rate, measured at the beginning of the night shortly after a meal is a good measure of the energy used for maintenance. The calculation of the total energy expenditure in young children is often based on the basal metabolic rate multiplied by a factor for activity. The latest FAO/WHO/UNU report found that in children the total energy expenditure, measured by doubly labeled water, was lower than estimated as basal metabolic rate, from Schofield equation, multiplied by the activity factor. This lower measured total energy expenditure, might either be due a lower amount of energy used for maintenance or to a lower level of activity as stated in the equation. Because we found in **chapter 5** higher values of physical activity level than given in the FAO/WHO/UNU report, 1.6 vs. 1.4 (29,30), it is unlikely that the lower values of TEE are due to a lower level of activity. More likely is that energy used for maintenance is overestimated by using equations for basal metabolic rate as measure of energy used for maintenance.

The difference between energy used for maintenance measured from the sleeping metabolic rate and from equations to estimate basal metabolic rate depended on the level of basal metabolic rate, and was higher at lower ranges of basal metabolic rate, indicating that energy expenditure was overestimated especially in children of younger age or lower weight. In the older and larger children, most close to the mean age for which the equations were developed, less discrepancy was found between measured and estimated energy used for maintenance. The published equations may lead to errors in the age group of 3 and 4 years; this might be due to the well-known phenomenon that the error increases at the boundaries of the population for which the prediction equation was developed.

We also measured fat mass and fat free mass, by the isotope dilution method. Energy used for maintenance and growth was positively correlated with fat free mass, but not with fat mass, indicating that energy needs in overweight children would be more overestimated than in normal weight children in equations based on weight only. When the estimated energy needs of young children are too high, incorrect dietary advice might be given to children, causing the risk to develop and maintain childhood overweight.

To assess the energy used for physical activity, accurate objective methods are needed to assess habitual free-living physical activity in young children. Indirect subjective methods such as parent/teacher questionnaires and parental recall (22,23) are not sufficiently validated for the assessment of physical activity in preschool children (23). Self-report, also a subjective method, is not recommended for children under the age of 10 (24). Alternatives that have been developed in the past years are direct methods such as accelerometers and pedometers, well validated methods include the doubly labeled water (DLW) method, heart rate monitoring and direct observation (23,25). In **chapter 5**, we assessed the validity evidence of the TracmorD, a tri axial accelerometer, to determine energy used for physical activity in 3 and 4 year old children. Total energy expenditure was measured using the doubly labeled water method. Sleeping metabolic rate, as a measure to asses energy used for maintenance, was measured by indirect calorimetry (Deltatrac). Physical activity level was calculated as total energy expenditure divided by sleeping metabolic rate. Energy used for activity was calculated as the difference between total and sleeping energy expenditure. We found that the TracmorD provides moderate-to-strong validity evidence that supports its use to evaluate energy used for physical activity in 3 and 4 year old children.

In this study we found that the total energy expenditure in our group of 3 and 4 year old children was 1301 ± 193 kcal/day. These average results are higher than the average values for total energy expenditure given in a table of the FAO/WHO/UNU report (29). This difference can be completely explained by the higher weight of the infants in our cohort (16.3 ± 1.9 kg) compared to the assumed average value in the table in the report (15 kg). When we calculated the total energy expenditure according to the formula presented by FAO/WHO/UNU in the report, we found no difference between our data and the data calculated according to the formula. The mean value according to our measurement is 1301 ± 193 kcal, compared to 1233 ± 100 kcal when calculated according to the FAO/WHO/UNU formula. We compared both the measured and the calculated data according to the Bland–Altman method and found no significant difference. So, we are convinced that our data on total energy expenditure are correct as they are in agreement with the FAO/WHO/UNU formula and calculated according to established methods.

The physical activity level is calculated as total energy divided by basal metabolic rate (the energy used for maintenance). In a previous report of the FAO/WHO/UNU a physical activity level of 1.4 was found (29), while we found a physical activity level of 1.6. As we found in **chapter 4** lower values for energy used for maintenance than calculated from the Schofield equation, as used in the FAO/WHO/UNU report, the resulting physical activity level is higher. We also like to focus the attention on the fact that in the FAO/WHO/UNU report only one mean value for the physical activity level is given for 3 and 4 year old children, while in older children differences are made between less and more active children. The data present in the report to calculate the physical activity level were insufficient to make a distinction between active and sedentary children, while we found a wide range in physical activity level from 1.2 to 2.1. This has high influence in the total energy expenditure, therefore also in young children, difference need to be made between active and sedentary children.

CONCLUSION PART I

The first objective was to validate and evaluate methods used to assess overweight, energy used for maintenance and energy used for physical activity in preschool children. The most valid instruments are also the most time consuming and most expensive methods. Measurement of BMI can give a misclassification of children in the overweight group, but it is the most feasible proxy measure for large groups and shows a significant correlation with body fat percentage. Basal metabolic rate equations in literature overestimate energy used for maintenance in 3 and 4 year old children. Tracmor$_D$ accelerometer provides moderate-to-strong validity evidence that supports its use to evaluate energy used for physical activity in 3 and 4 year old children.

PART II. ACTIVITY BEHAVIOR AND OVERWEIGHT IN PRESCHOOL CHILDREN

As mentioned before, in **chapter 2** a review is presented which showed that in previous literature an inverse relation between physical activity and body fat percentage was found, but we found that studies in young children were limited. In **chapter 6, 7 and 8** we assessed whether (aspects of) physical activity, sedentary behavior, sleep and parental factors are related to BMI in young children. In short, less time with the possibility to move unrestricted in infancy; more time watching television, shorter sleep duration, a higher parental BMI and less maternal active commuting are related to overweight.

Physical activity

In **chapter 6** we examined whether the time that an infant is able to move unrestrictedly and time spent in baby seats at age 9 months are related to weight and waist circumference at age 9 months and growth from 9 to 24 months. Weight and height were measured in Well Baby Clinics at the ages of 9 and 24 months. Time spent moving unrestricted and time spent in baby seats were reported on a questionnaire at age 9 months. Children born <37 weeks or with a low birth weight (<2500 g) were excluded. We found an inverse relation between the possibility to move freely at 9 months and the change in Z-scores weight-for-age and weight-for-height from 9 to 24 months of age. Our explanation for this finding is that the possibility to move may influence the amount of physical activity, which in turn increases the energy expenditure and thereby contribute to a more healthy growth pattern in weight-for-age or weigh-for-height.

In this longitudinal study we found a relation between infant movement opportunities and prospective change in weight-for-age and weight-for-height. However, in a review we found that physical activity may not be a key determinant of body fat gain in children (31), but only 6 studies in children aged 4-11 years were included. Therefore, more research in younger children is needed.

In **chapter 8** we examined the cross-sectional association between physical activity, measured by the TracmorD accelerometer, and BMI in children aged 2-5 years old and found an unexpected positive association. From the review in **chapter 2** we expected to find no relation between physical activity and BMI in children of this age, but the positive association was also found in 2 other studies in preschool children (32,33). Next to BMI as proxy measure for adiposity we used waist circumference as outcome measure. For waist circumference we found no association with children's physical activity. Different explanations are possible to explain these results in preschool children. First the relation can be dependent on age. A review of Jimenez-Pavon et al. (34) found that the relation between physical activity and adiposity was found more often with increasing age. The inverse relation was found in 60% (n = 3) of preschool studies; 77% (n = 17) of studies of primary school-age children, and 86% (n = 18) of studies of adolescents (34). In this review both proxies for adiposity (usually absolute BMI or BMI z-score) and more precise measures of adiposity (measures of body composition, such as dual-energy x-ray absorptiometry, skinfolds, impedance) were used as outcome measure. Secondly, as mentioned before, the reliability of BMI in this age group is uncertain. BMI is not only dependent on fat mass but also on muscle mass (10,11), so there is a possibility of misclassification of mild overweight. Since more children in the GECKO Drenthe cohort were overweight than obese, it is possible that misclassification for mild excess adiposity obscured the relation between BMI and physical activity.

Sedentary behavior

Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture (35). 1 MET (metabolic equivalent) is equal to resting metabolic rate during quiet sitting. MET scores of activities are multiples of the resting MET levels and range from 0.9 (sleeping) to 18 METs (running at 10.9 mph) (36). Physical activity may prevent the development of overweight by an increase in total energy expenditure due to an increase in muscle mass, which causes an increase in the basal metabolic rate and due to increased activity energy expenditure during and after the activity. While physical activity increases the energy expenditure, sedentary behavior can decrease the energy expenditure. More sedentary behavior may lead to less muscle mass, which is related to a lower basal metabolism, and to less energy expenditure spend for activity. In addition, some sedentary behaviors, like watching television, are related to less healthy eating patterns and a higher total energy intake (37). When this higher energy intake is not compensated by a higher energy expenditure, on the long term, overweight will develop. In **chapter 7** we investigated the interplay between screen time, sleep duration, outdoor play, having a television in the bedroom and the number of televisions at home and their association with BMI in 3 and 4 year old children. These factors might not only be associated to BMI, but also to each other. Therefore, a mediation model was used to estimate not only the effect of these factors on BMI, but it also takes into accounts the effect of the factors on each other. A mediation model links a putative cause to a presumed effect at least in part via an intermediary variable. Ordinary Least Square regression-based path analysis was used to estimate direct and indirect effects on BMI in mediation models with the PROCESS macro for SPSS. (Hayes, 2012, http://www.afhayes.com/). Television in the bedroom or number of televisions at home were dependent variables (causes); screen time and sleep duration were mediators; BMI was the outcome variable (effect); and gender was the covariate. We found that a television in the bedroom or more televisions at home gave a higher screen time. Both a direct relation of television watching with BMI, but also an indirect relation was found. A television in the bedroom or more televisions at home gave a higher screen time, which in turn decreased the sleep duration and resulted in higher BMI

Sleep duration

Sedentary behavior and physical activity directly influences the energy balance. In **chapter 7** we assessed whether sleep duration was associated with BMI in young children. In adults it is found that sleep duration influences the development of overweight by different mechanisms which influence both energy intake and energy expenditure. In children less is known about this relation and its underlying mechanisms. Sleep deprivation can cause a change in appetite regulating hormone levels, resulting in increased hunger and appetite (38-41). In children it is found that shorter sleep duration is associated with higher consumption of energy-rich foods (42). Secondly, in adults, shorter sleep duration is also associated with fatigue and reduced physical activity, resulting in less total energy expenditure (43,44). In children aged 3-5 years a positive relation is found between physical activity and sleep duration (45). Finally shorter sleep duration gives more opportunity to eat, especially in the evening after dinner (46-48). A study in 5-6 year old children found that eating snacks while watching TV was associated with a lower sleep duration, which gives a higher chance of being overweight (49). The results we found in **chapter 7** confirm the results found in adults: lower sleep duration is related to a higher

BMI. More time of watching television is association with less sleep duration, and both are associated with a higher BMI.

Parental influences on children's physical activity and BMI

During infancy and early childhood parents play an important role in the development of habits related to eating and physical activity. At that young age, parents can shape a healthy environment to encourage the development of a healthy diet and daily habitual physical activity patterns (50). In **chapter 8** we investigated if parental BMI and parental physical activity are related to physical activity, BMI and waist circumference in their 3 and 4 year old children. Parental physical activity was assessed by a validated questionnaire: SQUASH. The SQUASH is pre-structured in commuting activities, leisure time activities, sports, household activities, activities at work or school. Questions included type of activity, duration, frequency and intensity. Children's physical activity was assessed by TracmorD, a tri axial accelerometer. We found that the BMI of both parents is positively related to the BMI and waist circumference of their children and a higher maternal BMI was related to less physical activity of their children. Maternal active commuting was negatively related to BMI of the children. When a mother goes to her work by bike or walking, she will bring her child walking or biking with her to go to the school or daycare. These results might indicate that when mothers actively participate with their children in their daily physical activity it will contribute to a healthier BMI of their children. However, moderate physical activity in the mothers and total physical activity in the fathers was positively related to BMI of boys, but no association with children's waist circumference was found. Therefore, a reduction in the BMI of parents might be more helpful in stimulating activity and reducing overweight in young children than stimulation of the activity in the parents.

CONCLUSION PART II

The second objective of this thesis was to examine correlates of physical activity, sedentary behavior and overweight in preschool children. In order to prevent overweight and obesity in young children, promoting a healthy home environment seems to be more important than physically active parents as role model for activity. A healthy home environment includes possibilities for the child to move, parents actively participating in physical activity together with their children, healthy food patterns, sufficient time for sleeping and restricted time for screen activities.

CLINICAL IMPLICATIONS AND DIRECTIONS FOR FUTURE RESEARCH

In the Netherlands, young children visit the Well-baby Clinics 14 times between the age of 2 weeks and 4 years. For these clinics, a national uniform detection protocol for overweight and obesity is introduced. The methods, instruments and cut-offs to detect overweight and obesity are defined. However, no uniform protocol is available for the procedure after the detection of overweight or obesity. From this thesis we conclude that the ability to move unrestrictedly is associated with growth between 9 and 24 months. At the age of 3 and 4 years, a restricted amount of watching television, no television in the bedroom and enough sleep may be helpful to prevent an increase in BMI. Furthermore, physical activity is not inversely related to BMI, but it is related to body fat percentage. So, physical activity can contribute to a healthy body composition. Parental lifestyle, expressed in parental BMI and physical activity with their children, like active commuting, is also related to children's BMI. Before implementing these factors into the clinical setting, intervention studies are needed to confirm that these factors do prevent and/or treat overweight. Two of the already running intervention studies in the Netherlands to prevent overweight are 'Beweegkriebels' and 'eetplezier en beweegkriebels ouderworkshop' (http://www.loketgezondleven.nl/interventies/i-database/). The aim of the first study is to enhance the possibilities of physical activity in playing and an active lifestyle in young children (0-4 year) in the preschool period. The aim of the second study is to enhance parental awareness of their role in a healthy environment of their child. In future studies it is important that existing equations to define energy used for maintenance are not be used to estimate energy intake, because they overestimate resting energy expenditure in young children. Moreover, intervention studies need to focus on promoting a healthy home environment which includes possibilities for the child to move, parents actively participating in physical activity together with their children, healthy food patterns, sufficient time for sleeping and restricted time for screen activities.

Further research in the GECKO Drenthe study

Within the GECKO Drenthe cohort, children will participate till adulthood. In follow up of this thesis the tracking of physical activity is very important. We found no benefit of physical activity on children's BMI. Because both age and measurement method of adiposity could affect the outcome, in future research physical activity in the preschool period in relation with development of obesity later in childhood need to be analyzed. Based on this thesis measurement of body fat is better than measurement of BMI, waist circumference and waist-to-height ratio to define excess body fat. Therefore, in a subgroup, measures of body fat must be performed to be able to analyze the association between physical activity and body fat instead of BMI. Physical activity needs to be measured by accelerometers, like TracmorD. Finally, the determinants of physical activity must be investigated thoroughly as higher levels of physical activity are consistently and strongly associated with a range of health outcomes (51,52).

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Chapter 10

Summary
Samenvatting
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SUMMARY

The increased prevalence of young children's obesity has become a major issue. Obesity is the result of an imbalance between energy intake and energy consumption, causing an excess of fat storage. The non used energy will be stored as fat and a prolonged time of surplus energy will cause obesity. The etiology of obesity is multi-factorial, both different environmental and genetic factors may contribute to the development of obesity in early life. Childhood obesity has both short term effects (on the obese child) and long term effects (on the adult who was obese during childhood). There is evidence that obesity tracks from childhood to adolescence and adulthood and a large increase in weight between ages 2 to 7 years are associated with adolescent adiposity and metabolic syndrome and overweight and cardiometabolic risk factors in adulthood. Thus focus on the etiology of overweight in the preschool years (<5 years) is important.

One of the factors related to obesity is physical activity. Physical activity can be defined as any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level. The number of studies investigating the etiology of physical activity in preschool children is limited. Various reviews about the health benefits of physical activity in preschool children found evidence to support a positive relationship between increased or higher physical activity and better measures of health.

In **chapter 2** a review was performed to summarize existing literature on the association between directly assessed physical activity and adiposity in preschool children (age 1.5 to 6 years). From the 17 included studies we found that the association between physical activity and obesity seems to depend on the outcome measure of adiposity. In 60% (3/5) of the studies using percentage body fat an inverse significant relationship with physical activity was found against 18% (2/11) of the studies that used body mass index as method to assess adiposity.

In **chapter 3** it was assessed whether waist-to-height-ratio is a better estimate of body fat percentage and cardiometabolic risk factors than BMI or waist circumference in children aged 3 to 7 years old. We found that waist-to-height-ratio was not superior to waist circumference or BMI in estimating percentage body fat in normal weight (n = 61) and overweight/obese (n = 75) children. Also,

waist-to-height-ratio was not better correlated with cardiometabolic risk factors than waist circumference or BMI in overweight/obese children.

In **chapter 4** we compared energy requirements for maintenance, measured by indirect calorimetry against existing equations predicting these requirements in 3 and 4 year old children (n = 30). All existing equations showed a significant overestimation, ranging from +58 to +144 kcal/day, indicating an overestimation of 8-19%. This overestimation was higher in children with lower energy requirements. Sleeping metabolic rate was positively related to weight, height and fat free mass, but was not related to fat mass. Because we found that energy needs for maintenance were related to fat free mass, but not with fat mass, energy needs in overweight children may be overestimated more using equations based on weight only.

In **chapter 5** the validity evidence of the TracmorD to determine energy used for physical activity was assessed in 3 and 4 year old children (n = 30). Total energy expenditure was measured using the doubly labeled water method. Sleeping metabolic rate was measured by indirect calorimetry. Total energy expenditure and sleeping metabolic rate were used to calculate physical activity level and activity energy expenditure. Physical activity level and activity energy expenditure were compared to the physical activity as monitored by the tri axial accelerometer, TracmorD. We found that TracmorD provides moderate-to-strong validity evidence that supports its use to evaluate energy used for physical activity in 3 and 4 year old children.

In **chapter 6** it was examined whether the time that an infant was able to move unrestricted and time spent in baby seats were related to weight and waist circumference at age 9 months and growth from 9 to 24 months. When an infant had more time to move unrestricted they had a lower waist circumference Z-score at 9 months, and more decreased Z-scores weight-for-height and weight-for-age between the ages 9 and 24 months. For time spent in baby seats, 'never users' showed a decline in Z-score weight-for-height as compared to those who used baby seats. On the contrary, Z-score waist circumference-for-age declined in children sitting for 1 hour or more in baby seats. We concluded that more time spent moving unrestricted in infancy may contribute to a healthy growth pattern.

In **chapter 7** the interplay between screen time, sleep duration, outdoor play, having a TV in the bedroom and the number of TVs at home and their association with BMI in 3 and 4 year old children (n = 759) was investigated. A television in the bedroom or more televisions at home gave a higher screen time, which in turn decreased the sleep duration and resulted in higher BMI. In contrast to the direct effect of screen time, sleep duration and a television in the bedroom on BMI, no direct effect was found for outdoor play and number or televisions at home on BMI. We concluded that short sleep duration, long screen time, and a television in the bedroom contribute to the presence of overweight in children aged 3 and 4 years.

In **chapter 8** it was examined whether parental physical activity and parental BMI were associated with physical activity, BMI and waist circumference in children aged 2 to 5 years old. Higher maternal BMI was related to less children's physical activity, whereas more active commuting by the mother and a lower parental BMI were related to a lower BMI of the children. A healthier lifestyle of the parents may result in a healthier BMI of both children and parents.

Chapter 9 comprised the general discussion in which (i) methodological issues in the measurement of physical activity and overweight in preschool children and (ii) activity behavior and overweight in preschool children were extensively discussed. Also, the directions for further research were explored.

The most valid instruments to assess overweight, energy used for maintenance and energy used for physical activity in preschool children are also the most time consuming and most expensive methods. Measurement of BMI can give a misclassification of children in the overweight group, but it is the most feasible proxy measure for large groups and shows a significant correlation with body fat percentage. BMR equations in literature overestimate energy used for maintenance in 3 and 4 year old children. TracmorD accelerometer provides moderate-to-strong validity evidence that supports its use to evaluate energy used for physical activity in 3 and 4 year old children.

In order to prevent overweight and obesity in young children, promoting a healthy home environment seems to be more important than physically active parents as role model for activity. A healthy home environment includes possibilities for the child to the physical active, parents actively participating in physical activity together with their children, healthy food patterns, sufficient time for sleeping and restricted time for screen activities.

SAMENVATTING

De toegenomen prevalentie van obesitas in jonge kinderen is een groot probleem. Bij obesitas zijn de energie inname en het energieverbruik niet meer in balans. Doordat de energie inname groter is dan het energieverbruik, wordt het teveel aan energie opgeslagen als vet. Wanneer dit voor een langere periode gebeurt, zal dat leiden tot obesitas. De determinanten van obesitas zijn multi-dimensionaal, zowel de omgeving als genetische factoren kunnen bijdragen aan de ontwikkeling van obesitas op jonge leeftijd. Obesitas in kinderen heeft gevolgen op de korte termijn (op het kind) en gevolgen op lange termijn (op de volwassene die als kind obesitas had). Daarnaast hebben kinderen met obesitas een grote kans om hun obesitas te behouden in de pubertijd en op de volwassen leeftijd. Ook is een grote toename in gewicht tussen de leeftijd van 2 en 7 jaar geassocieerd met het vet percentage en het metabool syndroom tijdens de puberteit en met overgewicht en cardiometabole risicofactoren op volwassen leeftijd. Daarom is het belangrijk om onderzoek toe te spitsen op de determinanten van overgewicht op jonge leeftijd (< 5 jaar).

Een van de factoren die geassocieerd is met obesitas is lichamelijke activiteit. Lichamelijke activiteit kan worden gedefinieerd als lichamelijke beweging geproduceerd door de inkrimping van de skeletspieren die een toename van het energieverbruik geven boven het basale niveau. Het aantal studies dat onderzoek doet naar de determinanten van fysieke activiteit in jonge kinderen is beperkt. Wel zijn in jonge kinderen al meerdere gezondheidsvoordelen van lichamelijke activiteit gevonden. Dit geeft bewijs voor een positieve relatie tussen lichamelijke activiteit en een betere gezondheid.

In **hoofdstuk 2** werd de bestaande literatuur beschreven die de associatie tussen lichaamsbeweging (gemeten met objectieve maten) en overgewicht in jonge kinderen (leeftijd 1,5 tot 6 jaar) onderzoeken. Na samenvoeging van de studies (n = 17) vonden we dat het verband tussen lichaamsbeweging en overgewicht lijkt af te hangen van de manier waarop overgewicht wordt vastgesteld. In 60% (3/5) van de studies die vet percentage gebruikten als uitkomstmaat voor lichaamsvet, werd meer lichamelijke beweging geassocieerd met een lager vet percentage. Terwijl in slechts 18% (2/11) van de studies die BMI als uitkomstmaat gebruikten, meer lichamelijke beweging geassocieerd was met een lagere BMI.

In **hoofdstuk 3** werd beoordeeld of de buikomtrek-lengte ratio een betere schatting van het vet percentage en de cardiometabole risicofactoren geeft dan de buikomtrek of de BMI in kinderen van 3 t/m 7 jaar. We vonden dat buikomtrek-lengte ratio niet beter was dan buikomtrek of BMI in het schatten van het vet percentage in kinderen met een gezond gewicht (n = 61) en ook niet in kinderen met overgewicht of obesitas (n = 75) kinderen. Ook was buikomtrek-lengte ratio niet beter gecorreleerd met cardiometabole risicofactoren dan buikomtrek of BMI in kinderen met overgewicht of obesitas.

In **hoofdstuk 4** vergeleken we de energiebehoefte voor onderhoud, het basaal metabolisme, met bestaande formules die deze energiebehoefte voorspellen in kinderen op de leeftijd van 3 en 4 jaar (n = 30). Het basaal metabolisme werd gemeten door middel van indirecte calorimetrie. Alle bestaande formules toonden een aanzienlijke overschatting, variërend van +58 tot +144 kcal/dag, wat een overschatting van 8-19% aangeeft. Deze overschatting is hoger in de kinderen met een lagere energiebehoefte. Het basaal metabolisme was positief gerelateerd aan gewicht, lengte en vetvrije massa, maar was niet gerelateerd aan vet massa. Doordat de energiebehoefte niet gerelateerd is aan vet massa, maar wel aan vetvrije massa, zal de energiebehoefte in kinderen met overgewicht nog meer overschat worden met behulp van vergelijkingen die alleen gebaseerd zijn op gewicht.

In **hoofdstuk 5** werd geëvalueerd of de TracmorD een valide instrument is om de energie voor lichamelijke activiteit te meten in 3- en 4-jarige kinderen (n = 30). Het totale energieverbruik werd gemeten met behulp van de dubbel gelabeld water methode. Het energieverbruik tijdens de slaap werd gemeten met indirecte calorimetrie. Het totale energieverbruik en het energieverbruik tijdens de slaap werden gebruikt om het lichamelijke activiteitenniveau en het energieverbruik voor activiteit te berekenen. Het lichamelijke activiteitenniveau en het energieverbruik voor activiteit werden vergeleken met de lichamelijke activiteit, gemeten door de tri axiale versnellingsmeter, TracmorD. We vonden dat TracmorD een matig tot sterk valide instrument is, om de energie benodigd voor fysieke activiteit te meten in 3- en 4-jarige kinderen.

In **hoofdstuk 6** werd onderzocht of de tijd die een kind vrij kan bewegen en de tijd die een kind doorbrengt in een babystoeltje gerelateerd zijn aan gewicht en buikomtrek op de leeftijd van 9 maanden en op de groei van 9 tot 24 maanden. Wij vonden dat meer tijd om vrij te bewegen gerelateerd was aan een lagere buikomtrek Z-score op 9 maanden, en meer afnemende Z-scores gewicht-voor-lengte en gewicht-voor-leeftijd tussen de leeftijd van 9 en 24 maanden.

Kinderen die nooit in een babyzitje zaten, lieten een daling zien van de Z-score gewicht-voor-lengte in vergelijking met degenen die wel babyzitjes gebruikten. Maar, de buikomtrek Z-score daalde in kinderen die 1 uur of meer per dag in een babyzitje zaten, vergeleken met de kinderen die minder dan 1 uur per dag in een babyzitje zaten. Wij concludeerden dat meer tijd om vrij te bewegen kan bijdragen aan een gezond groeipatroon in kinderen van 0 tot 1 jaar.

In **hoofdstuk 7** werd de relatie tussen beeldschermtijd, slaapduur, buiten spelen, een televisie in de slaapkamer, het aantal televisies in het huis en BMI onderzocht in kinderen op de leeftijd van 3 en 4 jaar (n = 759). Een televisie in de slaapkamer of meer televisies in huis gaf een hogere beeldschermtijd, wat een lagere slaapduur tot gevolg had en resulteerde in een hogere BMI. In tegenstelling tot de directe invloed van beeldschermtijd, slaapduur en een televisie in de slaapkamer op de BMI, werd geen rechtstreekse relatie gevonden voor buiten spelen en het aantal televisies in huis met BMI. Wij concludeerden dat een korte slaapduur, een lange beeldschermtijd en een televisie in de slaapkamer kunnen bijdragen aan overgewicht in kinderen op de leeftijd van 3 en 4 jaar.

In **hoofdstuk 8** werd onderzocht of lichamelijke activiteit en BMI van de ouders geassocieerd is met lichamelijke activiteit, BMI en buikomtrek van hun 2- t/m 5-jarige kinderen. Wij vonden dat een hogere BMI van de moeder geassocieerd was met een lagere hoeveelheid lichamelijke activiteit in de kinderen. Verder waren meer tijd besteed aan actief woon-werk verkeer (op de fiets of lopend) van de moeder en een lagere BMI van de ouders geassocieerd met een lagere BMI van de kinderen. Er werd geen associatie gevonden tussen de totale hoeveelheid lichamelijke activiteit van de ouders met de lichamelijke activiteit, de BMI en de buikomtrek van de kinderen. Een gezondere levensstijl van de ouders kan leiden tot een gezondere BMI van zowel de kinderen als de ouders.

Hoofdstuk 9 omvatte de algemene discussie waarin (i) de methodologische kwesties bij het meten van lichamelijke activiteit en overgewicht in jonge kinderen werden besproken en (ii) de relatie tussen lichamelijke activiteit en overgewicht in jonge kinderen werden bediscussieerd. Ook werden ideeën voor vervolgonderzoek besproken.

De meest valide instrumenten voor het meten van overgewicht, het basaal metabolisme en van energie voor lichamelijke activiteit in jonge kinderen zijn ook de meest tijdrovende en duurste methoden.

- BMI meting van jonge kinderen kan een misclassificatie van kinderen met overgewicht geven, maar is de meest haalbare methode als proxy voor lichaamsvet in grote groepen en laat een goede correlatie zien met het vet percentage.
- Bestaande formules om het basaal metabolisme te berekenen geven een overschatting in 3- en 4-jarige kinderen.
- De versnellingsmeter Tracmor$_D$ is een matig tot sterk valide instrument voor het evalueren van de energie die wordt gebruikt voor lichamelijke activiteit in 3- en 4-jarige kinderen.

Om overgewicht en obesitas in jonge kinderen te voorkomen, lijkt bevordering van een gezonde thuis situatie belangrijker te zijn dan lichamelijk actieve ouders. Een gezonde thuis situatie bevat mogelijkheden voor het kind om vrij te bewegen, ouders die samen met hun kinderen actief deelnemen aan fysieke activiteit, een gezond voedingspatroon, voldoende slaapduur en een beperkte hoeveelheid beeldschermtijd.

DANKWOORD

In de afgelopen 3,5 jaar is er heel wat gebeurt, waar dit proefschrift het resultaat van is. Natuurlijk kon ik dit niet in mijn eentje volbrengen, daarom wil ik een aantal mensen bedanken die mij hierbij hebben geholpen.

Prof P.J.J. Sauer, beste Pieter, dank voor uw tijd in mijn promotieonderzoek als promotor. Wat voor dag het ook was, u vond altijd tijd om te reageren op mijn email met weer een versie van een manuscript. Ik kon altijd langskomen met mijn vragen. Ook had u er soms meer vertrouwen in dan ik, waardoor ik de motivatie weer vond om door te gaan.

Dr. E. Corpeleijn, beste Eva, dank voor je kritische blik op mijn onderzoek als copromotor. Door jou heb ik geleerd om op de juiste manier een onderzoek uit te voeren, te analyseren en op te schrijven. Ik zal onze gezellige overleggen, treinritjes en congressen missen.

Prof. R.P. Stolk, beste Ronald, dank voor je inbreng op een aantal manuscripten als promotor. Ik heb met veel plezier op 'jouw' afdeling gewerkt.

Beste leescommissie, prof. K. Westerterp, prof. R.A. Hira Sing en prof. C. Visscher, bedankt voor jullie tijd om dit proefschrift te lezen en te beoordelen.

Kim en Leanne, ik ben blij dat ik jullie mijn paranimfen kan noemen. Kim, ik moet nog steeds denken aan onze wazige hotelkamer in Rotterdam, wat uiteindelijk allemaal bleek mee te vallen. Ik zal je missen als kamergenootje. Leanne, als GECKO collega's gingen we samen naar Lyon waar het delen van een Franse (lees kleine) hotel kamer prima ging ondanks dat ik je nog niet zo goed kende. Ik zal de gezamenlijke praatjes en theetjes missen. Alle PhD frustraties kon ik bij jullie kwijt, even samen klagen helpt altijd. Dank voor jullie hulp bij mijn promotie.

Bedankt collega's van de afdeling Epidemiologie. In het bijzonder de 4^{e} verdieping en de 'lunch gang'. Ik begin de opmerkingen over mijn Friese uitspraken al bijna te missen. Leyla, thank you for being my roommate. Ook Aukje en Petra, bedankt voor jullie hulp bij allerlei praktische zaken.

Bedankt studenten: Shailing, Miriam, Tessa, Marjory, Ingrid, Carmen en Johanna. Dank voor jullie bijdrage voor het GECKO Drenthe onderzoek en dan voornamelijk voor jullie hulp met de beweegdata, de grappige verhalen en de lol die we hebben gehad.

Beste co-auteurs, Gianni, Henk, Koen, Carianne, Eryn, Annelies, Marjory en Imke, bedankt voor jullie hulp in materiaal, expertise, data(verzameling), syntaxen, aanvullingen en opmerkingen. Ook jullie ideeën zitten in dit proefschrift verwerkt.

Suzette, Diane, Bas en de anderen van TCC die zich bezig hebben gehouden met GECKO. Zonder jullie hulp had ik niet zo'n makkelijk overzichtelijk dataprogramma tot mijn beschikking gehad, waarbij de data die je genereert ook echt blijkt te kloppen.

Een goed proefschrift kan alleen tot stand komen wanneer werkuren voldoende worden afgewisseld met 'ik wil nu absoluut niet aan mijn werk denken' uren. Zonder mijn vrienden en familie was dit niet gelukt. Bedankt voor jullie afleiding en steun. Ook veel dank aan mijn ouders, zij zijn uiteindelijk de basis van dit alles.

Last, maar absoluut niet least: Bart, dank voor je liefde en steun. De verdediging zal een mooie dag zijn, maar ik kijk nog meer uit naar 'onze' dag later dit jaar!

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Anna Sijtsma was born in Dokkum, the Netherlands, on January 6th, 1986. In 2004 she graduated from secondary school at the Dockinga College in Dokkum. In September 2004, she started her study Human Movement Sciences at the University of Groningen. She obtained the bachelor degree in 2007, followed by the master degree in 2009 with a specialization in physical activity, aging and health. During her research master she performed her internship in 2008/2009 at the department of Pediatrics at the University Medical Center Groningen, supervised by Prof. Dr. A.F. Bos. She studied the ability of general movements at baby age to predict motor function at school age in healthy children. In January 2010 she started her PhD at the department of Epidemiology at the University Medical Center Groningen, which resulted in this thesis. Anna further developed her skills as a researcher by presenting at international conferences, by supervising trainees and by completing her training and supervision plan in the Graduate School of Medical Sciences SHARE.

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